PERINATAL RISK STRATIFICATION OF PRETERM NEONATES ≤ 34 WEEKS AND THEIR NEURODEVELOPMENTAL OUTCOMES AT ONE YEAR

Dissertation submitted to

THE TAMILNADU DR.MGR MEDICAL UNIVERSITY

In partial fulfilment of the regulations for the award of the degree of

D.M. (NEONATOLOGY)

2011 - 2014

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI

APRIL 2014

CERTIFICATE

This is to certify that the dissertation entitled **"PERINATAL RISK STRATIFICATION OF PRETERM NEONATES ≤ 34 WEEKS AND THEIR NEURODEVELOPMENTAL OUTCOMES AT ONE YEAR"** is a bonafide work done by **DR. MANIKUMAR S** under my guidance and supervision during the period between Sep 2012 – Mar 2014 towards the partial fulfilment of requirement for the award of **D.M. (Neonatology)** degree examination to be held in August 2014 by The Tamilnadu Dr.M.G.R. Medical University, Chennai.

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DECLARATION

I solemnly declare that this study title **"PERINATAL RISK STRATIFICATION OF PRETERM NEONATES ≤ 34 WEEKS AND THEIR NEURODEVELOPMENTAL OUTCOMES AT ONE YEAR"** was my original work in the Department of Neonatology, Institute of child health and hospital for children, Egmore, Chennai under the guidance and supervision of **PROF. J.KUMUTHA, MD, DCH,** Professor & Head of Department, Department of Neonatology, Madras Medical College, Chennai. This dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the university requirements for the award of the degree of D.M. (Neonatology).

Date:

Place: Chennai **DR. MANIKUMAR S**

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INSTITUTIONAL ETHICS COMMITTEE
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CERTIFICATE OF APPROVAL

To
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Dear S.Manikumar

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Perinatal risk stratification of preterm neonates≤34 weeks and their neurodevelopmental outcomes at one year" No.09072013.

The following members of Ethics Committee were present in the meeting held on 02.07.2013 conducted at Madras Medical College, Chennai -3.

1. Dr.G.SivaKumar, MS FICS FAIS --- Chairperson
2. Prof. R. Nandhini MD -- Member Secretary
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7. Thiru. S. Govindsamy. BABL -- Lawyer
8. Tmt. Arnold Saulina MA MSW -- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

R Nandini 12/7/13
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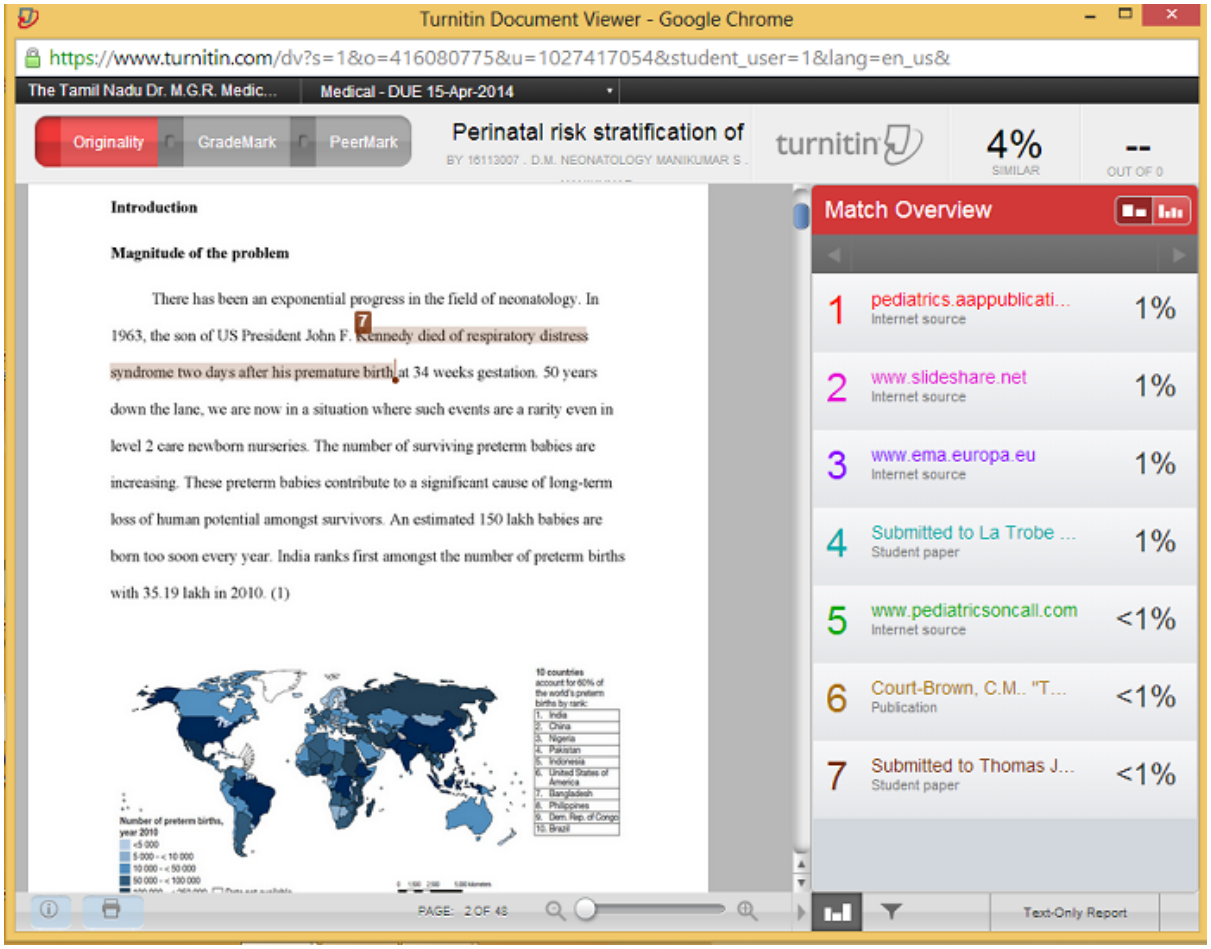
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There has been an exponential progress in the field of neonatology. In 1963, the son of US President John F. Kennedy died of respiratory distress syndrome two days after his premature birth at 34 weeks gestation. 50 years down the lane, we are now in a situation where such events are a rarity even in level 2 care newborn nurseries. The number of surviving preterm babies are increasing. These preterm babies contribute to a significant cause of long-term loss of human potential amongst survivors. An estimated 150 lakh babies are born too soon every year. India ranks first amongst the number of preterm births with 35.19 lakh in 2010. (1)
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INTRODUCTION

Introduction

Magnitude of the problem

There has been an exponential progress in the field of neonatology. In 1963, the son of US President John F. Kennedy died of respiratory distress syndrome two days after his premature birth at 34 weeks gestation. 50 years down the lane, we are now in a situation where such events are a rarity even in level 2 care newborn nurseries. The number of surviving preterm babies are increasing. These preterm babies contribute to a significant cause of long-term loss of human potential amongst survivors. An estimated 150 lakh babies are born too soon every year. India ranks first amongst the number of preterm births with 35.19 lakh in 2010. (1)

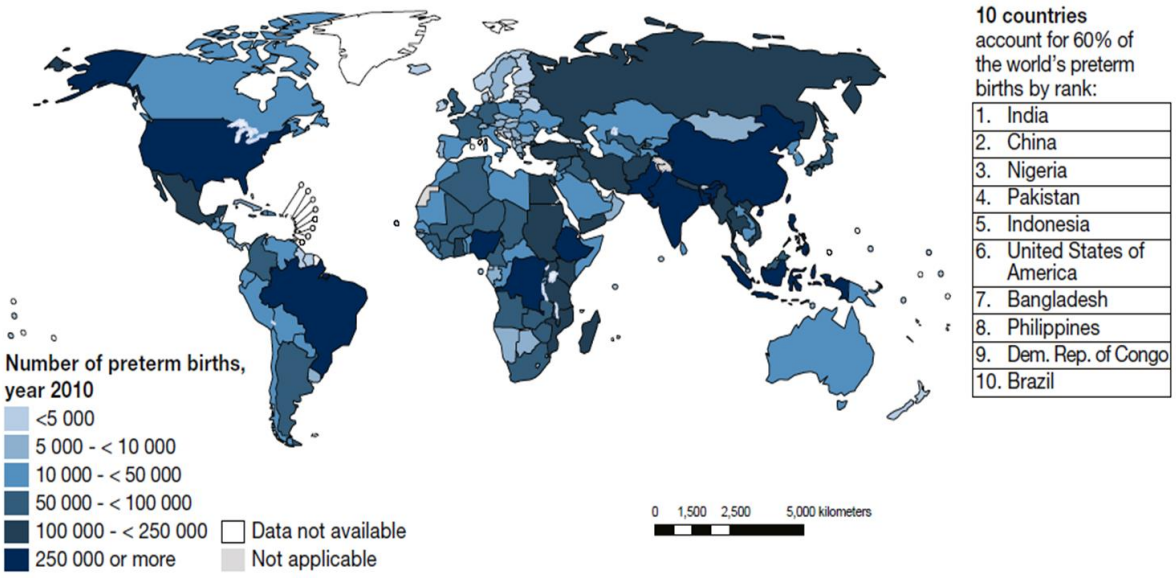


Fig 1: Number of preterm births in 2010 in the world

Intact survival

Survival of preterm babies is on the rise in India. Current neonatal interventions are focused on improving 'survival' of neonates. Though every attempt is made for 'intact survival' i.e. survival without disability, these preterm babies are at a substantial risk of future neurodevelopmental delay. Attention to long-term outcomes and minimizing disability is essential for optimal well-being.

The morbidities

The major adverse neurodevelopmental outcomes which can be associated with preterm birth include cerebral palsy, mental backwardness, blindness and deafness. Other than these, they are also at risk of various other minor morbidities like subtle tone abnormalities, poor cognitive and language functions, poor arithmetic skills, learning disabilities, refractory errors in the eye, hearing impairment, behavioural abnormalities, seizures and poor scholastic performance.(2-4) Some of these babies have multiple disabilities (5) and some of them may persist till school age (6, 7).

There has been a consistent association between motor functions at 12 months and cognitive functions at school age (8, 9). This is in consistence with Piaget's theory (Piaget J. The Origins of Intelligence in the Child. London, England: Penguin Educational; 1977), according to which the physical motor development lays the foundation for future cognitive development. The cognitive delays may not be obvious at an early age.

Factors that influence neurodevelopmental outcomes

The neurodevelopmental outcome of a preterm neonate is influenced by many antenatal factors, perinatal factors and neonatal factors. Some of the proven risk factors are as follows

Antenatal factors

Parent educational status and socioeconomic status

Previous preterm birth

Maternal anemia Hb<8 g%

Maternal malnutrition

Multiple gestation

Pre-eclampsia

Abnormal Doppler

Perinatal factors

Risks for early onset sepsis

Etiology of preterm birth

Gestational age at birth

Birth weight

IUGR / SGA

5” APGAR < 6

Acute intrapartum hypoxic events like cord complications and abruption

Incomplete or no antenatal steroids

Extramural delivery

Resuscitated at birth

Neonatal factors

Encephalopathy

Mechanical ventilation

Acute hypoxic events like air leaks, apnea requiring ventilation

Shock

Hypoglycemia

Sepsis

Significant Hyperbilirubunemia

NEC

BPD

PDA

Abnormal neurologic status at discharge

IVH

Abnormal neurosonogram

Growth delay

The outcome of preterm babies differ among various units. These differences are due to varied etiologies of prematurity, intrauterine environments, complications that occur during nursery stay, varied management protocols and home environment. Although there are various individual well conducted studies to prove that all the above mentioned risk factors are associated with poorer outcome, there is lack of studies to predict the outcome on a unified basis. Many studies that evaluated the demographic, prenatal, perinatal and neonatal predictors have failed to devise a method of predicting the outcome.

Early stimulation

The recent Cochrane review in 2012 by Spittle et.al. analysed 21 randomised controlled trials comprising 3133 preterm babies. They concluded that early intervention programmes for preterm infants have a positive influence on cognitive and motor outcomes during infancy, with the cognitive benefits persisting into pre-school age. Cognitive outcomes at 3 years improved by a standard mean difference (SMD) of 0.31 standard deviations (SD) in developmental quotient (DQ) and at pre-school age, intelligence quotient (IQ) improved by a SMD of 0.45 SD. The effect on motor outcomes though small was

significant, with a SMD of 0.10 SD in motor scale DQ. In spite of the heterogeneity between studies due to varied type and intensity of early developmental intervention programmes, they have consistently been found to modify neurodevelopmental outcome.(10)

Follow up of preterm babies

The follow up of preterm babies is not structured / standardized in most neonatal units. Stratification of preterm babies based on intra-uterine, perinatal and neonatal risks could possibly identify a group of babies at higher risk. Babies at lowest risk could be referred back to primary care and require less frequent assessment. Given the proven benefits of early stimulation, the risk approach will allow optimal utilization of limited, labour intensive, follow up services and optimize the early stimulation therapy to those babies at highest risk.

REVIEW OF LITERATURE

Review of literature

In a systematic review in 2012 published in The Lancet, there is ample evidence that intrauterine, perinatal and neonatal insults result in significant long-term neurological morbidity. The overall median risk of developing atleast one sequel was 39.4%. The studies included were especially from low and middle income countries. Although there is substantial heterogeneity among the included studies, it was found that in the analysed decade, the risk of development of neurologic sequelae has not changed over time (11). It is of particular interest that of the 28212 identified studies, only 153 were suitable for inclusion in the meta-analysis. Most had poor study methodology. So it is important to do a properly conducted study to extrapolate the findings to clinical use.

The preterm brain is vulnerable to various insults and they are at a higher risk of developing long term neurologic sequelae. Assessing the impact of antenatal, perinatal and neonatal factors on neurodevelopmental outcome requires a larger sample of preterm babies. This is made possible by neonatal networks in developed countries. The Vermont Oxford Network (VON), National Institute of Child Health and Human Development (NICHD) neonatal research network and the EPICure studies are prominent examples of it.

VON network

In this large multi-centric network study involving 33 centers, 8636 ELBW babies who were born from 1998-2003 were included. 6196 babies were discharged and among these only 3567 could be evaluated at 18-24 months corrected age. Severe disability was seen in 34%. Using multivariate logistic regression, the characteristics most highly associated with an increased risk of severe disability were cystic periventricular leukomalacia, severe intraventricular hemorrhage, 5 min Apgar ≤ 3, severe ROP, BPD, caregiver education < high school, male gender, cardiac compressions during resuscitation at birth, and decreasing birth weight. (12)

NICHD network

In this large multi-center cohort study by the NICHD neonatal research network, 7398 ELBW infants born between 1993 and 1998 were included in the study. 4761 survivors were followed up. 3903 infants could be evaluated at 18-22 months corrected age. Neurodevelopmental impairment was seen in 39.8% during 1993-94 which reduced to 27.8% during 1997-98. Logistic regression analysis showed that periventricular leukomalacia, BPD, multiple births, male gender, postnatal steroids, severe IVH, and poor maternal education were associated with poor neurodevelopmental outcome. Of the clinically relevant interventions analysed, postnatal steroids and high frequency ventilation were associated with increased risk of neurodevelopmental impairment. (13)

EPICure studies

In the EPICure study done in UK and Ireland in 1995, 811 infants <26 weeks of gestation were included. Only 314 babies (39%) survived. Survival without disability was 23%. These babies were followed up at 2.5, 6 and 11 years. Among these, 283 (92%) were assessed at 2.5 years, 241 (78%) at 6 years. Using step-wise logistic regression analysis, prolonged membrane rupture was associated with reduced cognition; abnormal neurosonogram and postnatal transfer were independently associated with severe motor disability. Nearly half had serious disability (14).

The EPICure 2 study is a prospective National cohort study involving 1031 surviving preterm infants <27 weeks of gestation born in 2006. 576 infants were followed up. This study showed that both the mortality as well as the long term neurodevelopmental outcome improved over time. Lower gestational age and male sex were associated with poorer neurodevelopmental outcome (15).

Local neonatal networks

In a follow up study of 205 VLBW babies in Germany, 142 were discharged (69.3%). Severe disability was diagnosed in 36 (25.4%) infants. Lower gestational age at birth and severe IVH were associated independently with severe disability. Also the difficulty in achieving high follow up rates even in a neonatal network is emphasized in that study (16).

Studies from developing countries

Neurodevelopmental outcome studies form resource limited settings may differ from the studies done in developed countries. Also the demographics of the preterm babies may differ probably related to suboptimal antenatal and perinatal care. Though there is a lack of well-established neonatal network in these countries, there are many well conducted follow up studies from individual centers.

In a single center follow up study of VLBW infants from Johannesburg, 314 infants were included in the study during 2006-07. 178 babies (56.6%) were discharged. 26 lost to follow up and 9 died post discharge. Of the remaining 143, Bayley Scale of Infant and Toddler Development Version III (BSID III) was done in 106 babies (74%) at a median age of 16.5 months. 23 infants had severe neurodevelopmental delay. The risk factors that are independently associated with poor outcome are duration of hospital stay, male gender, resuscitation at birth, hypothermia and cystic PVL (17).

In another similar study from a tertiary care hospital in Bangladesh published in 2006, 159 infants <33 weeks of gestation were enrolled. 16% died and 19% lost to follow up. More surprisingly, they have found a neurodevelopmental impairment in nearly two-thirds of infants. Socio-economic status assessed by family income and educational status had the most significant impact on post discharge mortality (18).

An unpublished pilot study on 225 preterm babies <33 weeks from a referral teaching NICU of south India has demonstrated that risk stratification identified 12.5 % babies as high risk who had had higher disability rates of 18% at one-year age (corrected for prematurity) and would benefit most by early stimulation. Most babies (87.5 %) had a risk of only 4.5 % (baseline) and could be assigned to limited follow up.

Study justification

Data from the western world cannot be directly extrapolated to our set up as the demographics may differ among population. There are also no well-established neonatal networks in India. Except for the one unpublished study from south India, we could not find any such studies in India. The primary reason for such a scenario in India is the lack of structured follow-up programs for preterm infants. This is probably the need of the hour in most neonatal care centers in India. In addition to standardizing follow up care services, the results of such a study will provide an opportunity for introspection and quality improvement of care process in the NICU. It also ensures optimal utilization of follow up services and maximal early stimulation therapy to those babies at highest risk. The infra-structure, manpower and medical management of preterm babies would differ from center to center and hence each center validation is necessary for the risk stratification tool.

AIMS AND OBJECTIVES

Purpose of the study

1. Standardization of follow up and early stimulation program for at-risk NICU babies
2. Assessment of magnitude of neurodevelopmental disability in preterm neonates
3. Association between intra-uterine insults, neonatal morbidities, management in NICU and developmental outcomes – an opportunity for standardization and quality improvement of care process in NICU
4. Evolving a tool that can be used in early neonatal period for prediction of developmental outcomes. This will be used for anticipatory guidance of parents and care givers and optimizing early stimulation and follow up services

Study Hypothesis

It is possible to make a prediction about an infant's neurodevelopmental outcome using a pre-discharge screening score, compiling intra-uterine and neonatal risk characteristics. It would help to optimize early intervention to those at higher risk and decrease the number of infants followed up in the lower risk group, thereby allowing best use of the limited available follow up resources.

Objectives of the study

Establishing a risk stratification tool (based on intra-uterine and neonatal insults) for predicting major neurodevelopmental disability (cerebral palsy, mental retardation, blindness, deafness) at one year (corrected for prematurity) in preterm babies (gestation <34 weeks).

MATERIALS AND METHODS

Setting:

The newborn units in Institute of Child Health and Hospital for Children and Institute of Obstetrics and Gynecology, Egmore. Both are tertiary level 3 care NICUs. The units have the necessary infra-structure, resources, man-power and protocols to provide optimal care to preterm babies. They have the necessary follow up services to provide standardized follow up care to the at-risk graduates.

Type of study:

Observational study: Prognostic study

Study period:

Enrollment period:

4 months: September 2012 – January 2013

Follow up period:

12 months age corrected for prematurity

Study protocol

Definitions of variables, outcomes, protocols for medical management and follow up were discussed with the Unit Heads and agreed upon to ensure uniformity of clinical management amongst the inborn and outborn Units. The NNF clinical practice guidelines are followed for individual case management.

Follow up team

The follow-up service has the following team members

1. Trained Neonatologist and allied medical specialists
2. Developmental physician

    Denver Developmental Screening Test

    Developmental assessment scale for indian infants - DASII

    CDC grading for major motor milestones

    Amiel Tison method of assessing tone

    Growth assessment based on WHO growth charts

3. Ophthalmologist

    ROP screening and therapy

    Refraction assessment

    Squint assessment

4. Audiologists and ENT surgeon, Speech therapist
5. Physical Medicine and Rehabilitation team

    Neurodevelopmental therapy

    Early intervention techniques

    Physiotherapy

Occupational therapy

6. Radiologist trained in neurosonography

7. Pediatric Neurologist

The principal investigator coordinated the follow up services. The principal investigator also underwent a training program for performing DASII (Developmental assessment scale for Indian infants) at Pune for 1 week.

The ophthalmologists from the Regional Institute of Ophthalmology (RIO) had regular visits to both of our intramural and extramural centers weekly once (on Saturdays in intramural center and on Wednesdays in extramural center). They performed ROP screening both for outpatients and for inpatients at the bedside.

If an infant required therapy for ROP, they are referred to RIO where facilities for laser photocoagulation and surgery for retinal detachment are also available. For hospitalized infants requiring therapy, the infants are transported in the neonatal 108 services accompanied by a neonatal resident trained in neonatal resuscitation.

Subjects:

- **Inclusion criteria**
  - All viable (>23 weeks and >400 grams birth weight) preterm babies (≤ 34 weeks gestation) admitted to the nursery and discharged after completion of neonatal care.
  - Both inborn and outborn babies who were referred in the first 48 hours of life (as babies referred later will not have accurate records of their initial NICU risk factors)
- **Exclusion criteria**
  - Babies with
    - major malformation
    - requiring major surgery
    - dysmorphism
  - Intrauterine infections
  - Babies referred out of the NICU to another hospital before completion of care
  - No consent from parents

Definition of outcomes

Primary outcome

- Death or Major Neurodevelopmental Disability (NDD) at 12 months corrected age
- Major developmental disability is defined as any one the following four:
  - Motor impairment
    - DASII motor score less than 70 at 1 year corrected age
  - Mental impairment
    - DASII mental score less than 70 at 1 year corrected age
  - Visual impairment
    - Blindness - complete loss of vision in one or both eyes
  - Hearing impairment
    - Profound hearing loss warranting assistive devices in one / both ears

Secondary outcome

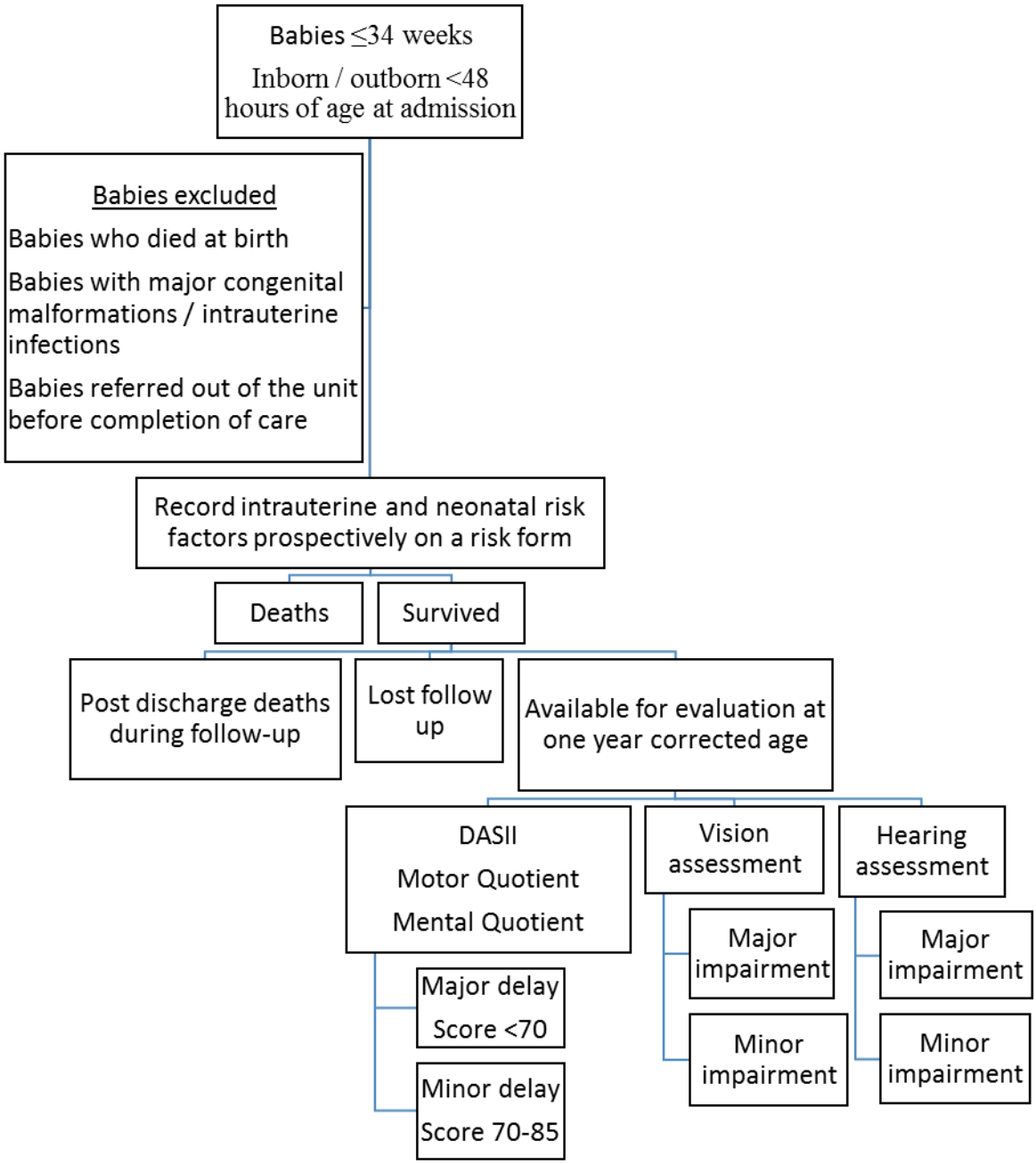
- Death or any neurodevelopmental disability (major or minor) at 12 months corrected age

- Minor Neurodevelopmental Disability is defined as any one of the following four at 12 months corrected age
    - Infants with DASII motor score of 70-85
    - Infants with DASII mental score of 70-85
    - Refractory error / Squint
    - Impaired hearing not requiring assistive devices.

End point in the study for enrolled baby

Follow up at 12 months age corrected for prematurity / death / discharged from NICU before completion of NICU care / lost to follow up.

Fig 2: Study flow diagram - protocol



For defining the primary outcome which is dichotomous, they are grouped as either death/major delay or minor/no delay.

Risk factors for neurodevelopmental outcomes

Intra-uterine insults and neonatal morbidities and management related issues associated with adverse neurodevelopment have been well described and their severity and association with outcomes previously published. The risk factors likely to affect neurodevelopment will be recorded from patient records on a structured form. The risk factors are classified according to their severity into various risk – categories.

Risk factors are recorded in a record form as follows

Baseline data

Gestational age (in weeks):

Birth weight (in grams):

Weight centile : $<3^{rd}$ / 3^{rd} -10^{th} / $>10^{th}$

Length centile: <3rd / 3rd -10th / $>10^{th}$

Head circumference centile : <3rd / 3rd -10th / $>10^{th}$

Antenatal data

Fetal well-being: normal / abnormal non-stress test/ biophysical profile <5

Risks for sepsis: maternal fever / pPROM / chorioamnionitis

Multifetal gestation: singleton / dichorionic / monochorionic twins / triplets / higher

Preeclampsia: absent / mild / severe

Doppler changes: cerebral redistribution / AREDF / not done

Perinatal data

Acute hypoxic events: abruption / cord prolapse / none

Antenatal steroids: dexamethasone / betamethasone

None / partial course / full course

Place of delivery: intramural / extramural

Resuscitation at birth: none / PPV / intubation / cardiac compressions

5" APGAR: <6 / >6

Neonatal data

Duration of ventilation: not ventilated / <3 days / 3-7 days / >7 days

Acute hypoxic events: air leaks / hypocarbia / apnea requiring resuscitation

Encephalopathy: absent / perinatal depression / HIE

Shock: absent / shock with normal BP / hypotensive shock

Hypoglycaemia: not present / asymptomatic / symptomatic / with seizures

Duration of hypoglycaemia: <3 days / >3 days

Sepsis: can't exclude / culture +ve sepsis / sepsis with hypotension or meningitis

Jaundice: none / needs phototherapy / needs exchange transfusion / has BIND

NEC: absent / stage 1/ stage 2/ stage 3

BPD: absent / mild / moderate / severe

PDA: not present / medical closure / surgical closure

IVH: not present / mild (grade 1/2) / severe (grade 3/4)

Neurosonogram: normal / ventriculomegaly / PVL

Neurological status at discharge: normal /abnormal

Assignment of risk:

The risk factors are classified as mild or moderate or severe based on the following table.

Table 1: Risk stratification criteria

	Mild risk	**Moderate risk**	**Severe risk**
Gestation	33 -34 weeks	30- 32 weeks	< 30 weeks
Birth weight	>1501 gm	1251 - 1500 gm	<1250 gm
Intra-uterine insults		Fetal growth 3^{rd} – 10^{th} centile Abnormal non-stress test or biophysical profile < 5 Maternal fever pPROM Dichorionic twins	Fetal growth <3^{rd} centile Severe maternal pre-eclampsia (seizures) Monochorionic twins / triplets or higher order Clinical chorioamnionitis Cord prolapse Abruption placenta Absent / reversed end diastolic flow
Antenatal steroids (ANS)		Incomplete course or < 24 hours from last dose	No antenatal steroids

Need for resuscitation at birth		Need for resuscitation (including positive pressure ventilation)	Need for extensive resuscitation (chest compressions, epinephrine)
Need for ventilation		Ventilation with normal blood gases and no air leaks	Ventilation abnormal blood gases and air leaks
Perfusion		Shock (poor perfusion) with normal blood pressure	Shock (poor perfusion) with hypotension
Shock therapy	Saline bolus	Inotropes	Steroids
Hypoglycemia		Hypoglycemia (asymptomatic)	Symptomatic hypoglycemia
Blood sugars		32 – 46 mg/dl	<32 mg/dl
Days of hypoglycemia		1-4 days	$\geq$ 5 days
IVH		IVH < grade III	Grade III IVH or ventriculomegaly, PVL
Infection	Can't exclude sepsis	Sepsis	Sepsis with hypotension / Meningitis
Neonatal jaundice	Requiring phototherapy	Requiring exchange transfusion	Has BIND
Hypothyroidism		Hypothyroidism	Treatment delayed (not normalized by one month)

Variable Definitions

Period of gestation:

The following order is taken for accurate assessment of gestational age

First trimester antenatal ultrasound scan at 6 to 12 weeks

Second trimester (upto 20 weeks) antenatal ultrasound scan

LMP based EDD

The extended new Ballards score

This will be also be used to estimate gestation if the neonatologist feels the baby's gestation appears different from the scan estimate. If the difference is more than 2 weeks, the extended New Ballard Score will be used to assign gestation.

Completed weeks of GA will be used for analysis.

Birth weight:

Measured using a 5-gram accuracy electronic weighing machine which is calibrated regularly (weekly)

Resuscitation guidelines at birth

NRP 2010 guidelines (19).

Ventilation – abnormal blood gases / air leaks

The duration of ventilation is recorded.

Acute hypoxic events include

Air leaks

Apnea requiring resuscitation

pCO_2 < 35 and > 65 mmHg in first 72 hours

Hypotension:

Mean blood pressure measured by non-invasive BP monitor < gestational age in weeks in 1st week, and <35 mm Hg after 1st week of life

Poor perfusion:

Tachycardia with altered alertness, poor capillary refill time, cool extremities, decreased urinary output (hypotension is a late sign of shock in neonates) (20)

Symptomatic hypoglycemia:

Blood sugar < 40 mg/dl with neuroglycopenic symptoms like jitteriness, seizures, lethargy, apnoea. The capillary blood glucose value must be confirmed atleast once with the laboratory value.

Neurosonogram:

Routine screening cranial ultrasonography is performed on all enrolled preterm babies once between 7 and 14 days of age and repeated at 40 weeks' postmenstrual age. It'll be done by the primary care neonatologist and confirmed by pediatric radiologist if abnormal. Intraventricular hemorrhage, if present is graded and noted. Periventricular leukomalacia and low-pressure ventriculomegaly, are included under abnormal neuro-sonogram. There is insufficient evidence for routine MRI of all VLBW preterm infants with abnormal results of cranial ultrasound(21). Hence it is not done for this study routinely for all babies

Sepsis:

Presence of at least two clinical symptoms and at least two laboratory signs (from the table below) in the presence of or as a result of suspected or proven infection (positive culture or microscopy) (22). This is endorsed by the report on the expert meeting on pediatric and neonatal sepsis, European medicines agency in June 2010. The details of the proposed definitions are attached in annexure 1.

If the clinical course is strongly suggestive of sepsis, and not fitting with the definitions as above, then the baby is categorized under clinical sepsis and if only screen is positive, the baby is treated till culture reports and categorized as "screen positive".

Neonatal jaundice:

The thresholds for phototherapy or exchange transfusion are from NICE protocol (23). Brainstem Evoked Response audiometry (BERA) is done for all babies who required exchange transfusion or has features of acute bilirubin encephalopathy. BIND scoring is not done as its classically seen only in late preterm and term babies.

Hypothyroidism:

In accordance with the AAP practice parameter, testing with TSH after 3 days and within 2 weeks of life (24). Values of TSH more than 20 would be investigated with free T4 also.

Neurodevelopmental screening and Follow-up schedule

The neurodevelopment screening and follow-up will be coordinated by the principal investigator. The neurological examination and interpretation of developmental assessment will be done by the principal investigator / pediatric neurologist if necessary. Efforts would be made to ensure follow up. Telephone numbers of both the parents are recorded.

Neurodevelopmental follow up is done at 4, 8 and 12 months of corrected gestational age. This categorization of age is primarily to facilitate assessment of major motor milestones by CDC grading. At every visit, screening is done with

DDST-2. Tone is assessed by Amiel-Tison method. Growth is assessed using WHO growth charts.

Babies with suspected neurodevelopment / neuro-sensory findings will be assessed more frequently and appropriate interventions initiated. Development Assessment Scale for Indian Infants (DASII) will be done at 12 months age corrected for prematurity. The MoQ (Motor Quotient) and MeQ (Mental Quotient) are documented.

Vision:

Retinopathy of prematurity (ROP) screen

Screening for ROP is performed in all enrolled neonates. The first retinal examination is performed not later than 4 weeks of age in infants born ≥ 28 weeks of gestational age. Infants born < 28 weeks or < 1200 grams birth weight are screened early, by 2-3 weeks of age, to enable early identification of Aggressive posterior ROP (AP-ROP). Findings will be recorded as per ICROP (International classification of ROP) (25).

Refraction and squint

Babies will be tested between 9-12 months corrected age for squint and refractory errors.

Hearing screen:

Distortion product Oto-acoustic emission (DPOAE) testing is done at discharge. Behavioural observation audiometry (BOA) is done within 3 months of life. BERA is done if DPOAE or BOA is abnormal. The tests will be carried out by audiologists.

Correcting for prematurity

The age of developmental follow up will be corrected for prematurity (full correction) – age for assessment will be calculated from the expected date of delivery (40 weeks).

Statistical methods

In the unpublished pilot study, there are 87.5 % babies at low risk (score 1,2) and 12.5 % with high risk (score or 3 or more) (1: 7 ratio of controls to cases). The proportion of babies with major neurodevelopmental delay (NDD) in low risk group was 4.5 % (0.045) and in the high risk group was 18 % (0.18). We will need to study 38 high –risk and 266 low- risk subjects to be able to reject the null hypothesis that the major NDD rates for high-risk and low-risk subjects are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. The sample size was calculated using an uncorrected chi-squared statistic.

Univariate analysis was used to compare risk variables and outcome at one year. Multiple logistic regressions were employed to find independent associations of risk categories with outcomes. Combination of risk factors were tested. A weighted risk score was evolved.

Ethics

Ethical clearance was obtained from the institutional ethics committee. The form is attached in appendix 1.

Consent

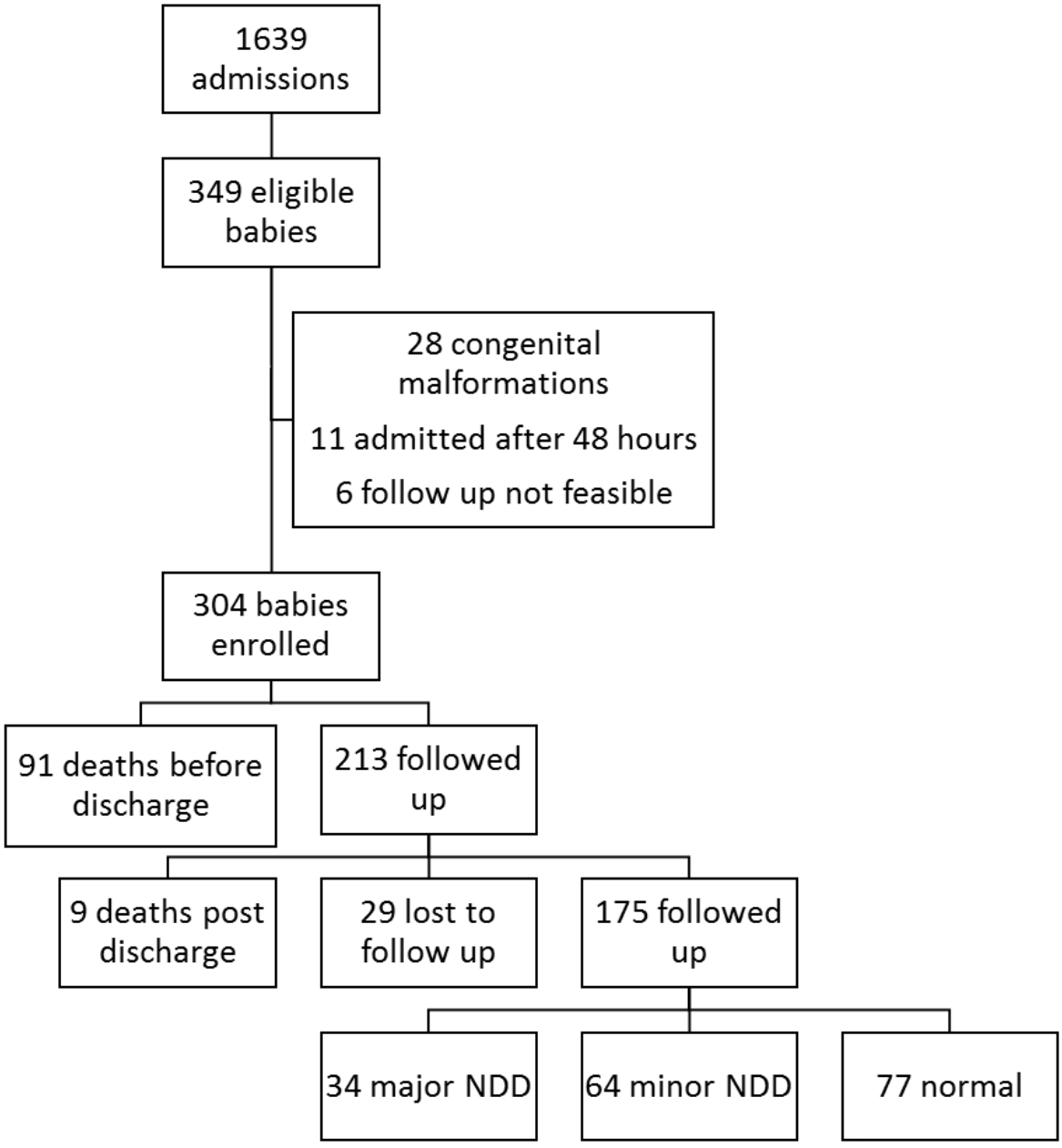
Permission to use patient data for research was obtained from the concerned intramural and extramural centers. The identity of patient was kept confidential. Patients refusing enrollment were offered the same follow up and early intervention as to enrolled babies.

OBSERVATION AND RESULTS

Results

There were 1639 babies who got admitted to the nursery during the enrollment period. Both inborn and outborn babies were included. During that enrollment period, 349 (21.3%) babies were preterm ≤34 weeks of gestation.

Fig 3: Study flow diagram



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28 babies had major malformations which can affect the neurodevelopment. 11 babies got admitted after 48 hours of life; these babies were excluded as the initial treatment data may not be available or is not standardised. 6 babies were excluded for non-feasibility of follow up. Non-feasibility of follow up was decided if referral has been from a distance more than 200 km from the Institution. After these exclusions, the remaining 304 babies were enrolled.

We had 91 deaths (29.9%) prior to discharge. All the remaining 213 were followed up. 29 (13.6%) babies were lost to follow up. Attempts were made to ensure maximal follow up through telephonic calls to both the parents or mails, which were sent to their corresponding house addresses. In spite of our efforts, we were unable to follow these 29 babies.

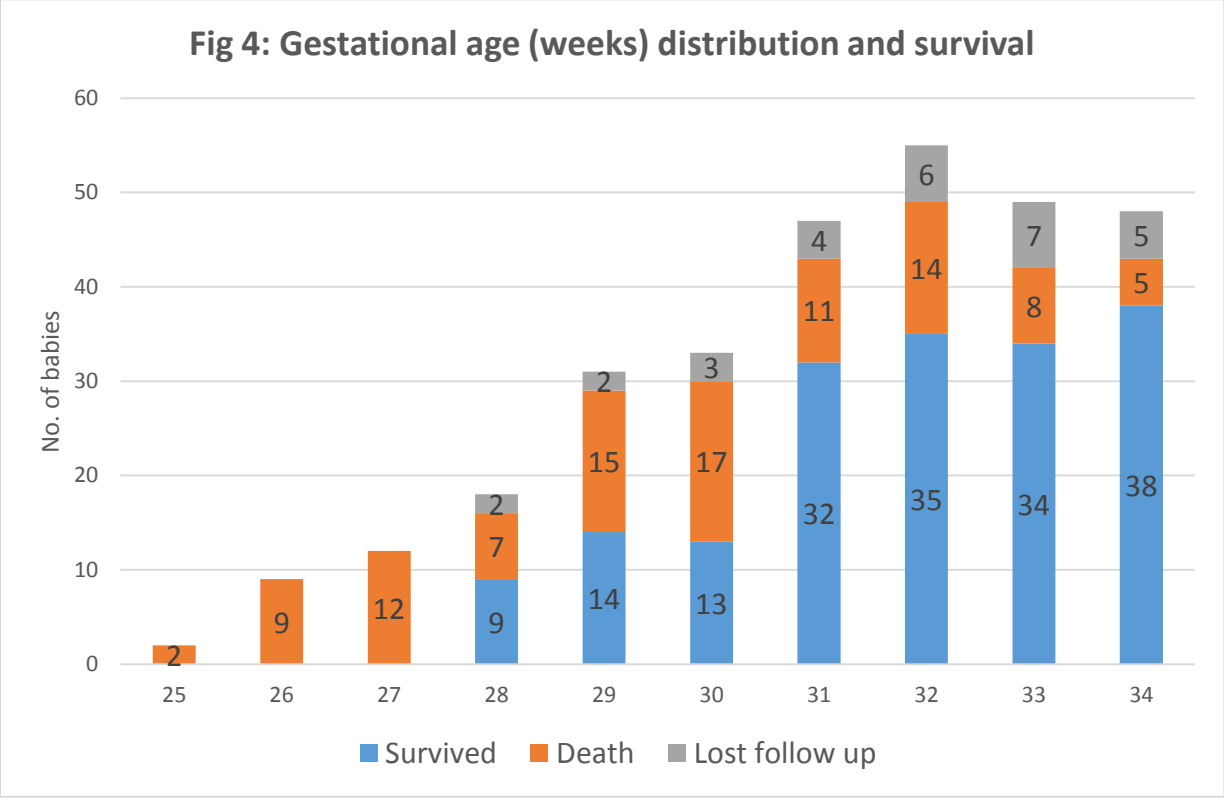
During follow up, 9 babies died within 3 months of discharge. All these 9 babies had growth delay. 5 of them had radiological evidence of pneumonia and had worsening respiratory illness prior to death. 2 had culture positive septicaemia. The remaining 2 died at home and had respiratory symptoms. The cause of death could not be ascertained clearly through telephonic conversation. The remaining 175 were followed up to 1 year of corrected age.

For defining the primary outcome, DASII, hearing and vision assessment were done at one year of corrected age. None of the babies had hearing

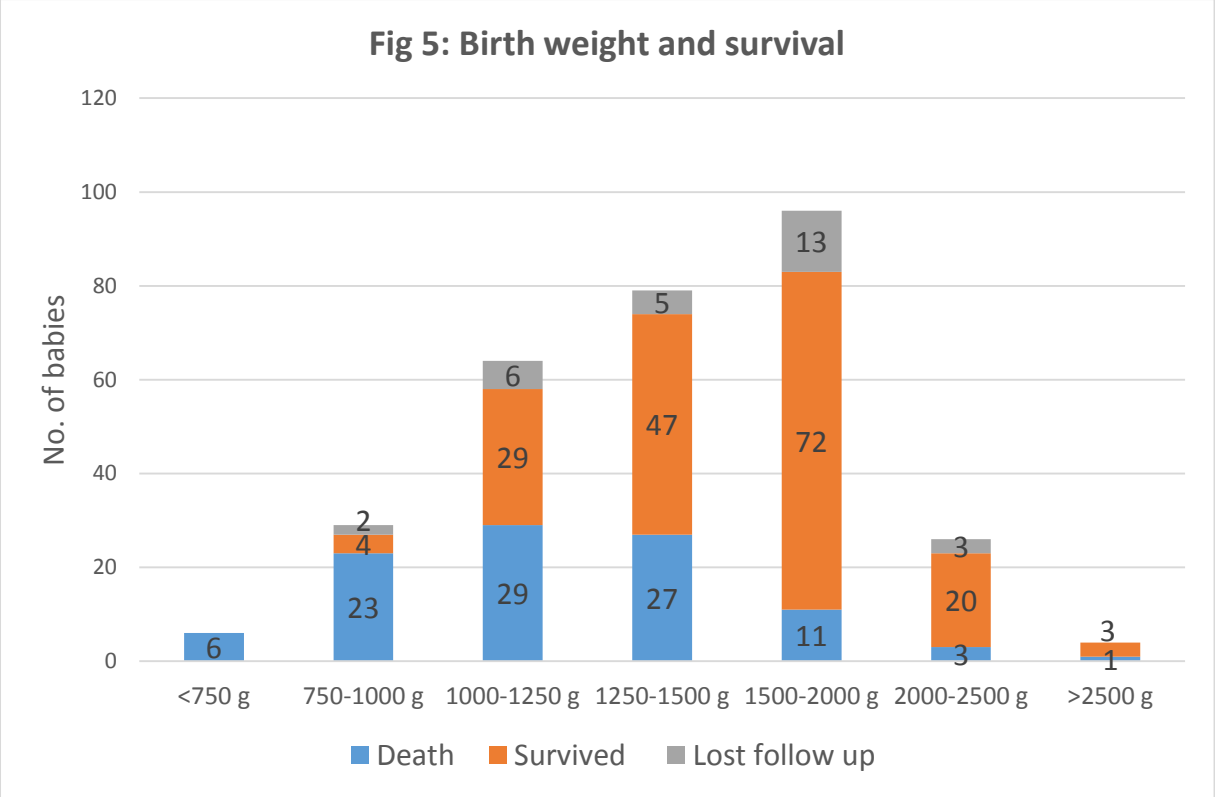
impairment requiring assistive hearing aids or complete blindness. The primary outcome is solely reflected by the motor and mental subsets of the developmental quotient assessed by DASII. The scenario with secondary outcome is also the same. None had hearing impairment. And also none had refractory errors requiring correction with glasses and only 2 babies had squint. Both these 2 babies had developmental delay as assessed by DASII. So the secondary outcome measures are also reflected purely by the outcomes as assessed by DASII.

Baseline distribution

The gestational age and birth weight distribution of the enrolled babies are depicted below in relation to survival outcome.

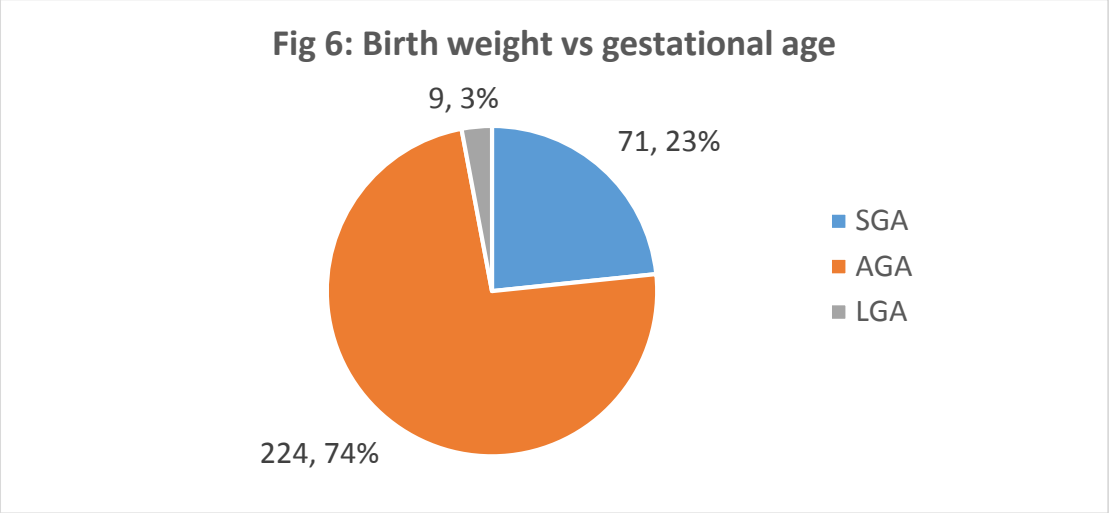


The survival of extreme preterm babies < 28 weeks of gestation (26.8%) or ELBW babies (17.1%) is very low. There were no survivors in ≤27 weeks of gestation in our study during the study period.

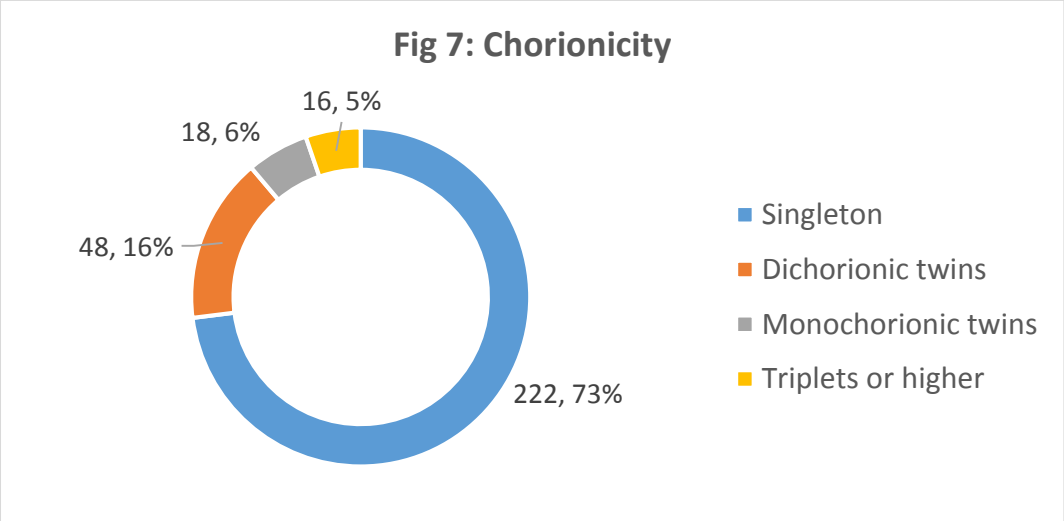


The birth weight data also suggests that the survival increases with increasing birth weight. There were no survivors in the incredibly low birth weight group (birth weight < 750 g).

There is also a high proportion of SGA babies (23%) in our study population. This is comparable with the national average of SGA babies in India. This should be taken into consideration before comparing birth weight data with other studies. Our population's lower birth weight infants may have higher proportion of higher gestational age infants.

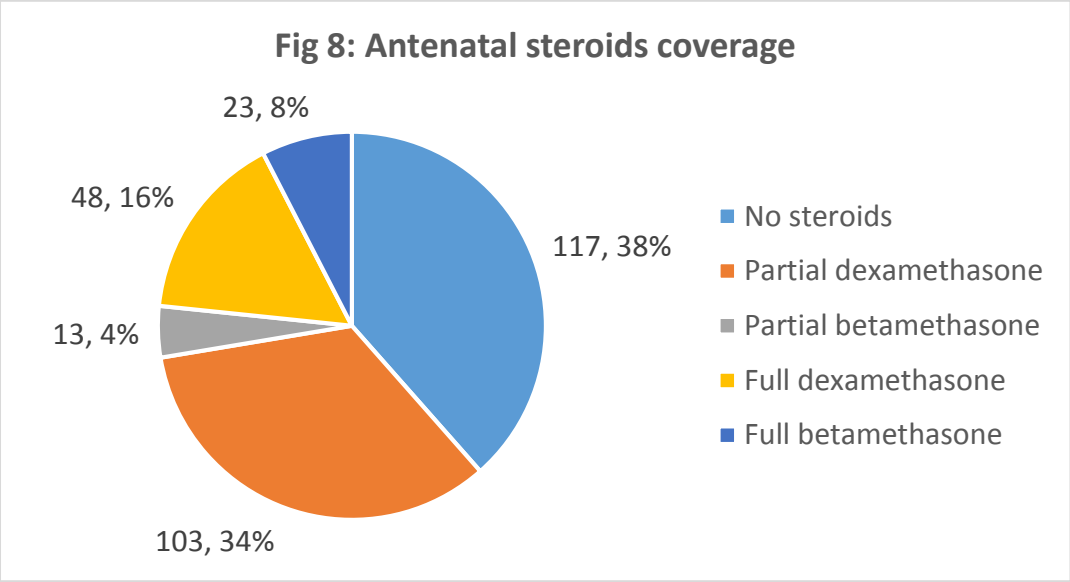


27% of our study population were a product of multi-fetal gestation. Except for 1 pregnancy, the rest of the multi-fetal gestations were a product of ovulation induction, done for infertility.

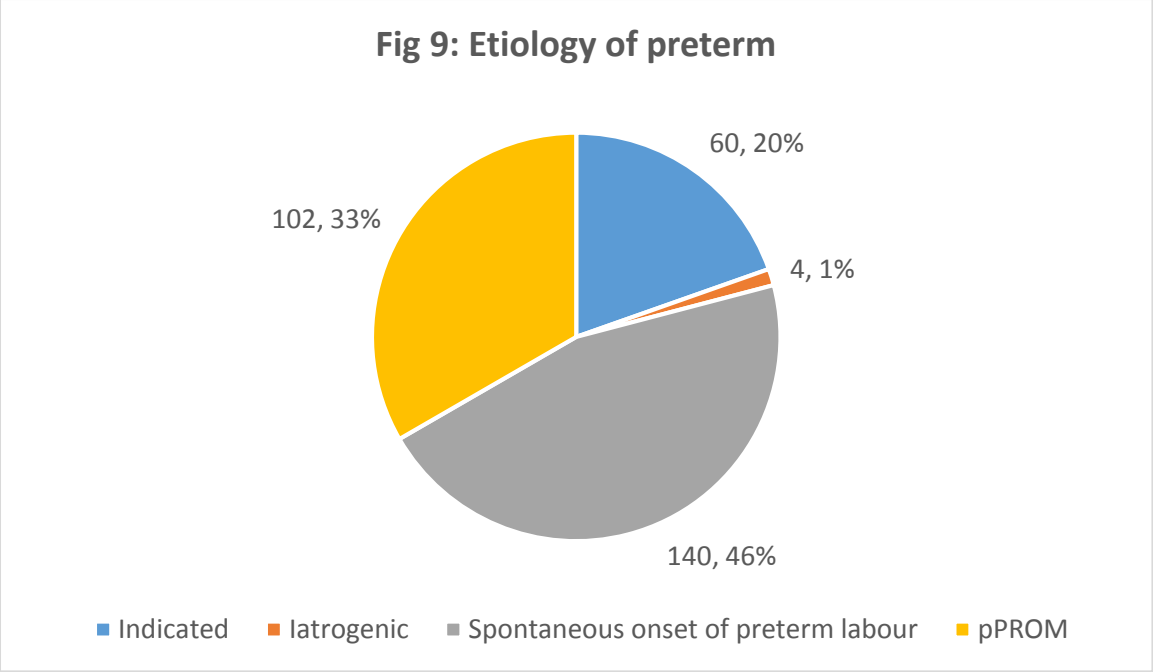


Antenatal steroids coverage is very low in our study population with only 24% being fully covered with steroids. 38% did not receive even a single dose of

steroid. In our inborn centre, dexamethasone phosphate is alone is administered, which is available free of cost to patients. Our study population also had 12% who were given betamethasone. These are administered to mothers prior to referral here. The high proportion of morbidities and mortalities may be partially attributed to the poor steroid coverage.



46% of our study population were born following spontaneous onset of preterm labour. 33% have preterm premature rupture of membranes. Also surprisingly, we had 4 babies who were induced based on wrong dates. In these 4 babies, prematurity was diagnosed only after the babies were born. These were categorised as ‘iatrogenic prematurity’. They are depicted in Fig 9.



The analysed risk factors and the prevalence of them in the study population are tabulated in table 2. Males predominate in our study population; 58.5% are males and 41.5% are females. There is also a high incidence of sepsis (60.7%). It is quite surprising that 76.6% had growth delay at 1 year.

Table 2: Prevalence of risk factors amongst study population

Risk factor	Prevalence n(%)
Parent education < middle school	12(6.5)
Gestational age ≤ 30 wks	98(35.6)
Primi / no previous preterm	210(76.4)
Maternal anemia Hb<8 g%	28(10.2)
Maternal malnutrition Wt<50 kg	85(30.9)
Risks for early onset sepsis	90(32.7)
IUGR	71(25.8)

Male sex	161(58.5)
SGA	62(22.5)
Birth weight < 1200 g	77(28.0)
5” APGAR < 6	45(16.4)
Indicated preterm	52(18.9)
Multiple gestation	75(27.3)
Acute intrapartum hypoxic events	32(11.6)
Pre-eclampsia	48(17.5)
Abnormal Doppler	132(48)
Incomplete / no antenatal steroids	208(75.6)
Extramural delivery	33(12.0)
Resuscitated at birth	73(26.5)
Encephalopathy	62(22.5)
Ventilated for > 3 days	68(40.7)
Acute hypoxic events	12(4.4)
Shock	119(43.3)
Hypoglycemia	23(8.4)
Sepsis	167(60.7)
Hyperbilirubunemia	151(54.9)
NEC	4(1.5)
BPD	2(1.1)
PDA	7(2.5)
Abnormal neurologic status at discharge	11(6.0)
IVH	34(12.4)
Abnormal neurosonogram	18(9.8)
Growth delay	134(76.6)

Outcomes

DASII at 1 year corrected age was performed for 175 babies. The results are tabulated below. There was a major delay in atleast one of Motor Quotient (MoQ) or Mental Quotient (MeQ) in 34 (19.2%) babies.

Table 3: DASII score results

DASII score n=175	Major delay Score <70	Minor delay Score 70-85	Normal Score >85
Motor Quotient (MoQ)	23	71	81
Mental Quotient (MeQ)	25	30	120
Any delay	34	64	77

Primary outcome

Death or major neurodevelopmental delay is seen in 134 babies (44.1%)

Table 4: Distribution of primary outcome

Death or Major NDD	134 (44.1%)
Normal or minor NDD	141 (46.4%)
Lost follow up	29 (9.5%)
Total	304

Table 5: Prevalence of primary outcome amongst risk factors

Risk factor	Prevalence % of death/major NDD if risk +	If absent
Parent education < middle school	23.8	16.7
Gestational age ≤ 30 wks	81.6	30.5
Primi / no previous preterm	52.9	35.4
Maternal anemia Hb<8 g%	50.0	48.6
Maternal malnutrition Wt<50 kg	40.0	52.6
Risks for early onset sepsis	36.7	54.6
IUGR	46.5	49.5
Male sex	50.9	45.6
SGA	41.9	50.7
Birth weight < 1200 g	79.2	36.9
5” APGAR < 6	86.7	41.3
Indicated preterm	51.9	48.0
Multiple gestation	36.0	53.5
Acute intrapartum hypoxic events	43.8	49.4
Pre-eclampsia	56.2	47.1
Abnormal Doppler	70.5	28.7
Incomplete / no antenatal steroids	51.0	41.8
Extramural delivery	30.3	51.2
Resuscitated at birth	74.0	39.6
Encephalopathy	66.1	43.7
Ventilated for > 3 days	64.7	83.8
Acute hypoxic events	91.7	46.8
Shock	94.1	14.1

Hypoglycemia	52.2	48.4
Sepsis	55.7	38.0
Hyperbilirubunemia	35.8	64.5
NEC	75.0	48.3
BPD	100	22.5
PDA	100	47.4
Abnormal neurologic status at discharge	100	18.5
IVH	79.4	44.6
Abnormal neurosonogram	88.9	16.3
Growth delay	24.6	2.4

The weighted risk score for death or major neurodevelopmental delay is tabulated in table 6. In the Univariate model, the risk factors associated with a composite outcome of death or major neurodevelopmental disability are presence of shock, abnormal neurosonogram, growth delay at 1 year, acute hypoxic events (like air leaks or apnea requiring resuscitation), gestational age <30 weeks, 5 minute APGAR <6, birth weight <1200 g, abnormal antenatal Doppler, abnormal neurologic status at discharge, IVH, BPD, requirement of resuscitation at birth, ventilatory requirements > 3 days, encephalopathy, PDA, sepsis, and previous preterm, in the order of strength of association. NEC, parent education <middle school, incomplete antenatal steroids, preeclampsia, male gender, indicated preterm, and hypoglycaemia are also having a trend towards poor primary outcome but they are statistically insignificant. Also of particular interest is the finding that multiple gestation, risks for early onset sepsis,

extramural delivery and hyperbilirubinemia are significantly associated with a better outcome.

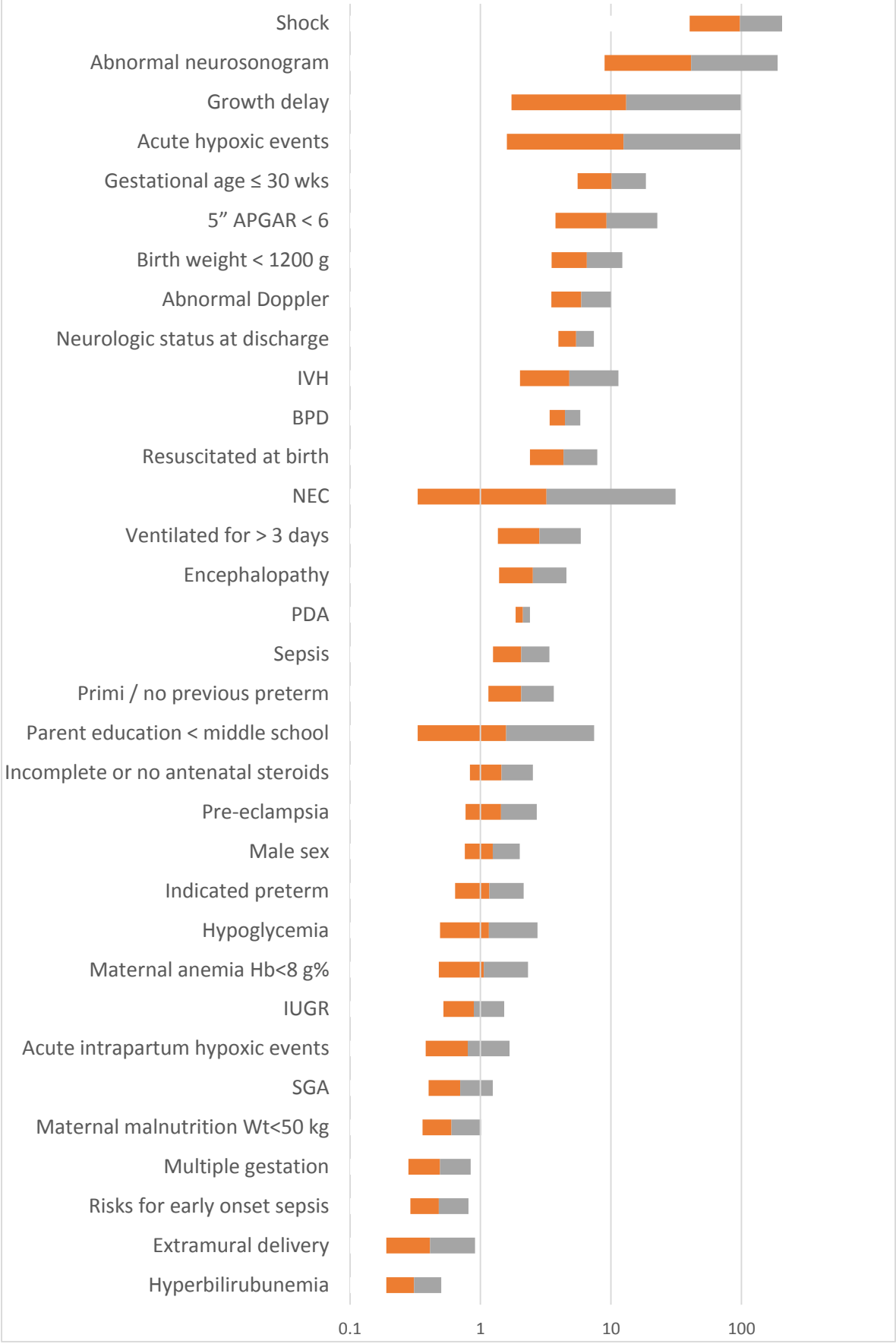
Table 6: Odds ratio for risk factors associated with poor primary outcome

Risk factor	Significance	Odds ratio	95% CI	
Parent education < middle school	0.73	1.57	0.33	7.43
Gestational age ≤ 30 wks	0.000	10.12	5.54	18.5
Primi / no previous preterm	0.02	2.05	1.15	3.64
Maternal anemia Hb<8 g%	1.00	1.06	0.48	2.31
Maternal malnutrition Wt<50 kg	0.07	0.60	0.36	1.01
Risks for early onset sepsis	0.007	0.48	0.29	0.81
IUGR	0.68	0.89	0.52	1.52
Male sex	0.39	1.24	0.76	2.00
SGA	0.25	0.70	0.40	1.24
Birth weight < 1200 g	0.000	6.53	3.51	12.2
5” APGAR < 6	0.000	9.24	3.76	22.7
Indicated preterm	0.65	1.17	0.64	2.14
Multiple gestation	0.01	0.49	0.28	0.84
Acute intrapartum hypoxic events	0.58	0.80	0.38	1.67
Pre-eclampsia	0.27	1.44	0.77	2.70
Abnormal Doppler	0.000	5.93	3.5	10.0
Incomplete / no antenatal steroids	0.21	1.45	0.83	2.52
Extramural delivery	0.03	0.41	0.19	0.91
Resuscitated at birth	0.000	4.33	2.39	7.85
Encephalopathy	0.002	2.52	1.39	4.55
Ventilated for > 3 days	0.006	2.83	1.36	5.88

Acute hypoxic events	0.002	12.5	1.59	98.4
Shock	0.000	97.5	40.1	237
Hypoglycemia	0.83	1.16	0.49	2.73
Sepsis	0.005	2.05	1.25	3.37
Hyperbilirubinemia	0.000	0.31	0.19	0.50
NEC	0.36	3.2	0.33	31.2
BPD	0.054	4.44	3.39	5.81
PDA	0.006	2.11	1.86	2.39
Neurologic status at discharge	0.000	5.41	3.95	7.39
IVH	0.000	4.79	2.01	11.4
Abnormal neurosonogram	0.000	41.2	8.95	189
Growth delay	0.003	13.1	1.73	98.8

This is represented in a logarithmic scale in fig. 10. Odds ratio > 1 indicates a significant association with a poorer outcome and <1 indicates a significant association with a better outcome.

Fig. 10: Primary outcome odds ratio for risk factors



Using a step-wise multiple regression analysis, the following risk factors are independently associated with a poor outcome. A regression equation can be constructed with these 4 risk factors to predict the probability of a poorer final outcome.

Table 7: Multi-step regression analyses of risk factors vs primary outcome

Risk factor	Sig.	Exp(B)
5” APGAR	0.000	0.084
Shock	0.000	0.027
Sepsis	0.05	0.405
Gestational age	0.000	0.195
Constant	0.000	14.723

Gestational age came as a better predictor of poorer neurodevelopmental outcome than birth weight.

Secondary outcome

Table 8: Distribution of secondary outcome

Death or any NDD	198 (65.2%)
Normal	77 (25.3%)
Lost follow up	29 (9.5%)
Total	304

Death or any neurodevelopmental delay is seen in 198 babies (65.2%).

Table 9: Prevalence of primary outcome amongst risk factors

Risk factor	Prevalence % of any NDD if risk factor +	If absent
Parent education < middle school	23.8	16.7
Gestational age ≤ 30 wks	81.6	30.5
Primi / no previous preterm	52.9	35.4
Maternal anemia Hb<8 g%	50.0	48.6
Maternal malnutrition Wt<50 kg	40.0	52.6
Risks for early onset sepsis	36.7	54.6
IUGR	46.5	49.5
Male sex	50.9	45.6
SGA	41.9	50.7
Birth weight < 1200 g	79.2	36.9
5” APGAR < 6	86.7	41.3
Indicated preterm	51.9	48.0
Multiple gestation	36.0	53.5
Acute intrapartum hypoxic events	43.8	49.4
Pre-eclampsia	56.2	47.1
Abnormal Doppler	70.5	28.7
Incomplete/ no antenatal steroids	51.0	41.8
Extramural delivery	30.3	51.2
Resuscitated at birth	74.0	39.6
Encephalopathy	66.1	43.7
Ventilated for > 3 days	64.7	83.8
Acute hypoxic events	91.7	46.8

Shock	94.1	14.1
Hypoglycemia	52.2	48.4
Sepsis	55.7	38.0
Hyperbilirubunemia	35.8	64.5
NEC	75.0	48.3
BPD	100	22.5
PDA	100	47.4
Abnormal neurologic status at discharge	100	18.5
IVH	79.4	44.6
Abnormal neurosonogram	88.9	16.3
Growth delay	24.6	2.4

The weighted risk score for secondary outcome is tabulated in table 10.

Table 10: Odds ratio for risk factors associated with poor secondary outcome

Risk factor	p value	Odds ratio	95% CI	
Parent education < middle school	0.25	0.44	0.11	1.7
Gestational age ≤ 30 wks	0	16.5	5.8	47
Primi / no previous preterm	0.02	2.1	1.2	3.7
Maternal anemia Hb<8 g%	1	0.9	0.4	2.3
Maternal malnutrition Wt<50 kg	0.15	0.6	0.4	1.1
Risks for early onset sepsis	0.03	0.5	0.3	0.9
IUGR	0	4	1.8	8.9
Male sex	0.4	1.3	0.7	2.1
SGA	0	4.7	1.9	11
Birth weight < 1200 g	0	6.6	2.7	16
5” APGAR < 6	0	10	2.5	44
Indicated preterm	0.01	2.9	1.3	6.8

Multiple gestation	0.17	1.6	0.9	3
Acute intrapartum hypoxic events	0.53	1.4	0.6	3.5
Pre-eclampsia	0.01	3.2	1.3	7.8
Abnormal Doppler	0	5.4	2.9	10
Incomplete / no antenatal steroids	1	1	0.6	1.9
Extramural delivery	0.06	0.5	0.2	1
Resuscitated at birth	0.001	3.6	1.7	7.7
Encephalopathy	0.01	2.7	1.3	5.9
Ventilated for > 3 days	0.05	3.2	1.1	9.9
Acute hypoxic events	0.04	1.4	1.3	1.5
Shock	0	1.9	1.7	2.3
Hypoglycemia	0.14	2.8	0.8	9.6
Sepsis	0.002	2.4	1.4	4.1
Hyperbilirubinemia	0.6	1.2	0.7	2
NEC	0.3	1.4	1.3	1.5
BPD	0.5	1.7	1.5	1.9
PDA	0.2	1.4	1.3	1.5
Neurologic status at discharge	0.003	1.8	1.6	2.1
IVH	0	1.5	1.3	1.6
Abnormal neurosonogram	0	1.9	1.6	2.1
Growth delay	0	30	8.9	106

They are depicted in a logarithmic scale in fig. 11. The results are comparable with the primary outcome with a few exceptions. Hyperbilirubinemia which had a negative association with primary outcome, is positively associated with a composite outcome of death or any neurodevelopmental delay but the association is insignificant.

Fig 11: Secondary outcome - odds for risk factors

Risks for early onset sepsis (maternal fever or pPROM or chorioamnionitis) is the only risk factor which is not associated with a poorer neurodevelopmental outcome.

DISCUSSION

Discussion

The outcome is analysed at 1 year in our study though the babies are still continuing in our follow up. Our primary outcome is chosen only as 'major' neurodevelopmental delay because at 1 year, some of the subtle minor outcomes have not yet manifested and / or some are over-estimated which can disappear over time due to plasticity of the brain. For analysing major neurodevelopmental delays, 1 year follow up is acceptable. It has been found that earlier outcome at 12-24 months has 87% correlation with outcome at 8 years and also during adolescence (8, 26, 27). The cognitive outcomes are known to worsen through ages 1 to 4 years (9). Though the initial neuromotor status lays the foundation for future cognitive development according to Piaget's theory, the correlation may not be accurate. The outcome is more favourable in 10% and less favourable in 7% at 5 years in a study be Veen at.al. in 1991 (28). In a study by Astbury et.al. , it was found that the neurodevelopmental delay also may be under-estimated at 1 year of age (29). Voss et.al. have concluded that atleast 6 year outcome may be necessary to derive meaningful conclusions (30). Also catch-up growth has yet to occur fully in our study. We are still following up our babies and further follow up may throw more light to our findings.

The proportion of preterm neonates ≤ 34 weeks in our centre is 21.3%. This is high primarily because ours is a referral tertiary care (level 3) centre for primary and secondary care centres in and around Chennai. There are rapid

advances in primary neonatal care through CEmONC (Comprehensive Emergency Obstetric and Newborn Care) centres in Tamil Nadu. Only high risk mothers and neonates who cannot be managed there, get referred to our Institute.

The incidence of death or major neurodevelopmental delay, which is the primary outcome in our study is 44.1%. Most of the studies from the western world even some decades ago, have a very low incidence of poor neurologic outcome of <20% (31). But studies from the developing world are entirely different. In a study from Bangladesh in 2006, the incidence is 68% in <33 weeks preterm babies (18). Because of these huge differences, it might be difficult to extrapolate their risks to our population. This justifies our study at our centre.

Gestational age is one of the independent major determinant of poor outcome with a mean odds ratio of 10.1. The effects remained significant even after multiple logistic regression. This has been documented in many previous studies. In a 2012 review by Xiong et.al., gestational age has been the consistent independent risk factor for poor outcome (32). In a study by Andrews et. al. in 2008, IQ was found to increase by 1.9 points for each week of gestational age (33). Though birth weight too had an odds ratio of 6.5, it didn't come as an independent risk factor for poor outcome.

Most of our babies had growth delay at 1 year of corrected age. This implies that catch up growth is still not complete. Our study has a 23% incidence of SGA babies. The odds ratio for growth delay is 13.1. This correlation of growth

delay with poor neuro-developmental outcome was documented in earlier studies too (34, 35). In a study by Neubauer et.al., the head size at 3 months was strongly associated with poor neurodevelopmental outcome assessed by BSID at 24 months. The catch up growth can even be delayed up to 8-14 years of age (36). Our growth restricted babies also had a typical developmental pattern of more of motor delay than mental delay. In a study by Shah et. al., post natal growth failure was significantly associated with psychomotor delay (p=0.006) but not with cognitive delay (p=0.379) (37). Our findings are also very similar. These findings are partly attributed to hypotonia and muscular weakness associated with growth delay.

Abnormal neurosonogram (cPVL - cystic periventricular leukomalacia) is one of the consistent poor prognostic indicator in previous similar studies. The odds ratio in univariate analysis is 41.2 which is the highest amongst the risk factors. Almost all the studies have similar findings. In the VON network study(12), the odds ratio is 5.56 for cPVL and it has the highest predictive ability for a poorer outcome. In a study by Fazzi et.al. in 1992, it was found that the sonographic abnormalities correlated more closely with neuromotor delay rather than cognitive delay(38). Our study had predicted worser outcome in both the domains. This is in concurrence with the study by Ballot et.al. in a developing country(17), where it is associated with a poorer outcome in all domains.

5 minute APGAR score < 6 has an odds ratio of 9.24 for predicting death or major neurodevelopmental delay. In the VON network study (12), the adjusted odds ratio is 2.06 for severe delay. In our study, it is also one of the independent predictor of a composite outcome of death or major delay.

Male gender is associated with a poorer outcome. Regression analyses has shown it to be an independent predictor of long term poorer outcome in all the network studies (VON, NICHD and EPICure studies) and also in a study done by Stoelhorst et.al. (39). But in our study, though there is a trend towards poorer outcome, this is not statistically significant. This might be because of the gender bias prevailing in the community of our study population. Male babies, even when they had mild illness gets referred early due to this bias and hence the relatively better outcome when compared with other studies.

Neonatal hyperbilirubinemia is surprisingly associated with a better neurologic outcome. In a study by Van de Bor et.al. in 1992 (40), it was found that the odds ratio for neurodevelopmental impairment is 1.84 if associated with severe IVH and 1.05 if without severe IVH. Only 12.4% of our population had any grade of IVH and only 1.5% had severe IVH. This is partly due to the fact that we use dexamethasone as the preferred choice of antenatal steroid which is known to be protective for IVH. So most didn't have severe IVH and hence the the subset of population with both severe IVH and hyperbilirubinemia is very small in number. That's probably the reason why hyperbilirubinemia is not

associated with death or major neurodevelopmental delay. But it is associated with minor neurodevelopmental delay though not statistically significant.

Overall, the strongest association with a poor neurologic outcome with an odds ratio of >10 is seen with abnormal neurosonogram, gestational age <30 weeks, growth delay and acute hypoxic events which include air leaks, apnea requiring resuscitation and shock.

Strengths of the study

This is one of the large single center follow up study. Our institute is the apex tertiary care center for all government hospitals in Tamil nadu. So the findings of our study can be reasonably extrapolated to the whole of Tamil nadu.

We have established a standardised follow up care program in both the intramural and extramural center. This will provide the platform for future studies on neurodevelopmental follow up of babies discharged from our nursery.

There is no inter-observer variability in the outcomes analysed as the principal investigator has done all the neurodevelopmental outcome assessment by DASII.

There are only 13.6% drop-outs from the study, who lost follow up. This is within the acceptable limits of <20%. So the clinical findings of this study may be considered reliable.

Limitations of the study

This short period of follow-up is one of our primary limitation. The study cohort is still under follow up and further long term follow up of these babies may throw more light on accurate interpretation of data.

Implications for clinical use

Based on the odds ratio for each risk factor, the clinician can estimate the risk of future neurodevelopmental delay at discharge itself. This will help in

intensifying follow up and early intervention programs for those babies identified to be in high risk for neurodevelopmental impairment. On a simpler note, just assessing the 4 independent predictors – 5 minute APGAR <6, shock, sepsis and gestational age <30 weeks, itself can predict to a reasonable extent a poorer outcome. This can be used as a community tool to identify a subset of babies with highest risk. These babies require frequent follow up services and can aid the government in implementing benefit programmes for such high risk babies.

CONCLUSION

Conclusion

Establishing a standardized follow up program with provision for early intervention is advised for all newborn nurseries who care for preterm babies <34 weeks of gestation.

Gestational age ≤30 weeks, 5 minute APGAR <6, presence of sepsis and shock are independent risk factors for poor composite outcome of death or major neurodevelopmental delay at 1 year of corrected age.

Gestational age ≤30 weeks, acute hypoxic events (air leaks, apnea requiring resuscitation, hypocapnia), growth delay, abnormal neurosonogram at 40 weeks and shock are associated with an odds ratio >10 for a poor composite outcome of death or major neurodevelopmental delay at 1 year of corrected age.

Catch-up growth of preterm babies <34 weeks is inadequate at 1 year of corrected age.

Long term follow-up is necessary to accurately assess the impact of antenatal, perinatal and neonatal risk factors on neurodevelopment.

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ANNEXURES

Annexure 1: Clinical signs and laboratory signs for sepsis

Clinical signs	**Laboratory signs**
Temperature instability / hypothermia / hyperthermia Cardiovascular instability (heart rate variations, oliguria, hypotension, poor perfusion) Skin and subcutaneous lesions (petechiae, sclerema) Respiratory instability (apnea, tachypnea, increasing FIO2 requirements or ventilatory support) Gastrointestinal instability (feed intolerance, poor suck, abdominal distension) Non-specific (irritability, lethargy, hypotonia)	Leukopenia / Leukocytosis Thrombocytopenia CRP positive Hypoglycemia / hyperglycemia despite normal glucose intake Metabolic acidosis

Annexure 2: Excel code sheet of patient data

Explanation of the codes

Parent education

1=Profession or honours

2=Graduate or post graduate

3=Intermediate or post high school diploma

4=High school certificate

5=Middle school certificate

6=Primary school certificate

Parity

1=primi

2=previous 2nd/3rd trimester fetal loss

3=previous preterm

4=no previous adverse events

Maternal anemia

1=Hb<6

2=6-8

3=>8

4=normal

Maternal malnutrition

1=wt <50 kg

2=>50 kg

Risks for sepsis

1=none

2=pPROM

3=maternal fever

4=clinical chorioamnionitis

5=2+3

6=2+4

Intrauterine growth

1=no IUGR

2=asymmetric IUGR

3=symmetric IUGR

Sex

1=male

2=female

SGA

1=SGA

2=AGA

3=LGA

5" APGAR

1=>6

2=4-6

3=<4

Etiology of preterm

1=spontaneous preterm labour

2=pPROM

3=indicated preterm

4=iatrogenic (wrong dates)

Twins

1=singleton

2=dichorionic twin

3=monochorionic twin

4=triplets or higher

Acute intrapartum events

1=none

2=fetal distress

3=cord complications

4=abruption

Preeclampsia

1=none

2=preeclampsia

3=severe preeclampsia

Abnormal Doppler

1=normal

2=cerebral redistribution

3=AREDF

4=not done

A/N steroids

1=no steroids

2=partial course dexa

3=partial course beta

4=full course dexa

5=full course beta

Place of delivery

1=intramural

2=extramural

Resuscitation at birth

1=none

2=requires PPV

3=requires intubation

4=requires chest compression

Encephalopathy

1=none

2=perinatal depression

3=HIE stage 1

4=stage 2

5=stage 3

Duration of ventilation

1=not ventilated

2=<3days

3=3-7 days

4=>7 days

Acute hypoxic events

1=none

2=air leaks

3=apnea requiring resuscitation

4=both

Shock

1=no shock

2=fluid responsive

3=catecholamine responsive

4=catecholamine resistant

Hypoglycemia

1=no hypoglycemia

2=<25 mg%

3=>3 days

4=symptomatic

5=asymp >25 and <3d

Sepsis

1=no sepsis

2=screen positive

3=culture positive

4=clinical sepsis

Jaundice

1=no jaundice

2=requires phototherapy

3=requires exchange

4=has BIND

NEC

1=no NEC

2=stage 1

3=stage 2

4=stage 3

CLD

1=no BPD

2=mild BPD

3=modearte BPD

4=severe BPD

PDA

1=no PDA

2=closed medically

3=closed surgically

Neurologic status at discharge

1= normal

2= abnormal

IVH

1= no IVH

2=grade 1

3=grade 2

4=grade 3

PVL

1=normal

2=abnormal

4,8 & 12 month examination

1=abnormal Denver

2=abnormal tone

3=abnormal CDC grading

4=1+2

5=1+3

6=2+3

7=1+2+3

8=normal

DASII MoQ or MeQ

1= score < 70

2= 70-85

3= >85

Vision

1=blindness

2=refractory error / squint

3=no impairment

ROP

1=requires surgery

2=requires LASER

3=no treatment required

4=no ROP

Hearing

1=requiring assistive devices

2=not requiring devices

3=no impairment

Growth delay

1= normal

2= grade 1 PEM

3= grade 2

4= grade 3

5= grade 4

Hypothyroidism

1= present

2= absent

Death

1=death

2=survived

3=lost follow up

Name	Parent education (best)	Gestational age (weeks)	Parity	Maternal anemia	Maternal malnutrition	Risks for sepsis	Abnormal Intrauterine growth	Sex	SGA	Birth weight (grams)	5" APGAR	Etiology of preterm	Twins	Acute intrapartum hypoxic events	Preeclampsia
Padmavathy	6	28	4	3	1	1	1	1	2	910	1	3	1	2	2
Kowsalya	5	34	2	3	1	1	2	2	1	1220	1	3	1	4	2
Rabiya	5	33	1	3	2	1	1	1	2	1760	1	1	1	3	1
Mahalakshmi 2	2	29	1	4	2	1	1	1	2	1245	1	1	2	1	1
Anusya	2	27	1	3	2	1	1	1	2	1075	1	1	1	1	1
Vijayalakshmi 3	5	34	1	3	2	1	2	2	1	1425	2	3	4	1	2
Ilamathi 3	5	33	2	4	2	1	1	1	1	1000	2	3	4	1	3
Kavitha 1	5	34	1	4	2	2	2	1	1	1235	1	2	4	1	1
Sivagami	5	33	2	3	1	2	1	2	2	1980	1	2	1	1	1
Yasmin		32	1	3	2	1	1	1	2	2160	1	3	1	1	1
Mumtaj Begum		32	1	3	1	1	2	1	1	1155	1	3	1	1	3
Shakila		29	4	3	2	1	1	2	2	1320	3	3	1	4	3
Vimala		29	1	3	2	2	1	1	2	1250	3	2	1	1	1
Rohini		32	1	2	1	1	2	2	1	1065	1	3	1	2	2
Sheela		26	1	3	2	1	1	1	2	935	2	1	1	1	1
Amudha 1		29	1	3	2	2	1	2	2	1065	1	2	3	1	1
Selvi		31	2	3	2	2	2	1	1	1160	1	2	1	1	1
Rohini		30	1	2	1	1	2	2	1	880	1	3	1	1	3
Kiran		27	1	3	2	2	1	2	2	890	3	2	1	1	1
Booma 3		27	1	3	2	2	1	2	2	860	1	2	4	1	1
Booma 1		27	1	3	2	2	2	1	1	700	2	2	4	1	1
Booma 4		27	1	3	2	2	2	1	1	765	1	2	4	1	1
Gulsar		29	1	3	2	1	1	2	2	995	2	3	1	1	3
Rosy		30	1	3	2	1	1	1	2	1325	1	1	1	1	1
Janani 2		31	1	3	2	1	1	1	2	1470	1	3	1	4	1
Sangeetha		26	1	3	1	2	1	1	2	765	3	2	1	1	1
Sudha		33	1	3	2	2	1	2	2	1580	1	2	1	1	1
Roshan bee		33	2	2	1	1	2	2	1	1285	1	3	1	1	1
Sripriya		32	1	3	2	1	2	2	2	1260	3	3	1	2	3
Hasena		30	4	3	2	1	2	1	2	1105	2	2	1	1	1
Karpagam		27	2	3	2	1	2	2	2	945	1	1	1	1	1
Jayanthi		27	1	3	2	1	1	1	2	1030	1	1	1	2	1
Nirmala		30	1	3	2	1	1	2	2	1845	1	1	1	1	1
Vidhyalakshmi 3		28	1	3	2	1	1	1	2	1195	2	1	4	1	1
Vedhavalli		30	1	2	1	1	2	2	1	710	1	3	1	1	3
Priyadharshini		26	1	3	2	1	1	1	2	980	3	1	1	1	1
Amala		29	2	3	2	1	1	2	2	1285	1	2	3	1	1
Lalitha		29	1	3	2	1	1	1	2	1000	1	1	1	1	1
Aswini		29	1	3	2	2	1	1	2	1140	1	1	1	1	1

Lakshmi		27	1	3	2	2	1	1	2	1105	1	1	1	1	1
Revathi 2		32	1	3	2	1	1	1	2	1230	1	1	2	1	1
Sangeetha 1		32	1	3	2	1	2	1	1	1240	1	2	2	1	1
Clara sundari		31	1	3	2	1	1	1	2	1805	1	1	1	1	1
Gnanasoundari		31	1	3	2	1	1	1	2	1710	1	1	1	1	1
Sandhya		32	1	3	2	1	1	1	2	1330	1	1	1	1	1
Lavanya		29	1	3	2	1	1	1	2	1150	1	1	1	1	1
Uma 1		30	1	3	1	1	2	1	1	975	1	1	2	1	1
Uma 2		30	1	3	2	1	2	1	2	1060	1	1	1	1	1
Bhuvaneswari 1		25	1	3	1	1	1	2	2	810	1	1	1	1	1
Bhuvaneswari 2		25	1	3	1	1	1	2	2	855	1	1	1	1	1
Divya		30	1	3	2	1	1	2	2	1140	1	1	1	1	1
Bhanvani		32	1	3	2	2	1	2	2	1400	3	1	1	1	1
Vijayammal		34	1	3	2	1	2	2	2	2030	1	1	1	1	1
Malathi		29	1	3	2	1	1	1	2	1275	3	1	1	1	1
Padmavathy		28	1	3	1	1	1	1	2	915	1	1	1	1	1
Venmathi		32	1	3	2	1	1	1	2	1480	1	2	1	1	1
Tamilarasi 2		32	1	3	1	1	2	1	1	770	1	1	3	1	1
Anjalai		31	1	3	2	1	1	1	2	1410	3	1	1	1	1
Rukmani		30	1	3	1	1	2	1	1	975	1	1	1	1	1
Sukartha		30	1	3	2	1	1	1	2	1485	3	1	1	1	1
Jansi		26	1	3	2	1	1	1	2	910	3	1	1	1	1
Dhanaselvi		34	1	3	2	1	1	2	2	2380	1	1	1	1	1
Zakiri		28	1	3	2	1	1	2	2	935	1	2	1	1	1
Yasmin		32	1	3	2	1	1	2	2	1780	1	1	1	1	1
Punitha		27	1	3	2	1	1	2	2	1195	1	2	1	1	1
Regina		28	1	3	2	1	1	1	2	1035	1	1	1	1	1
Sundari		27	1	3	2	1	1	1	2	825	1	1	1	1	1
Sumathi		28	1	3	2	1	1	1	2	965	1	1	1	1	1
Bama		30	1	3	1	1	1	2	2	1165	1	3	1	2	3
Karthigaselvi		28	2	3	2	1	1	1	2	1180	2	3	1	4	1
Bharathi 1		29	1	3	2	1	1	1	3	1740	1	1	3	1	1
Devipriya		31	1	4	2	1	1	2	2	1640	3	1	1	1	3
Ammu		30	2	3	2	1	1	1	2	1330	1	1	1	1	1
Bharathi 2		29	1	3	2	1	1	1	2	1130	1	1	3	1	1
Menaka devi		32	1	4	2	1	1	1	2	1475	3	1	1	1	3
Chandrakala 1		31	1	3	2	1	2	1	1	760	1	1	1	1	3
Chitra 2		32	1	3	1	1	2	1	1	1070	1	1	1	1	3
Priya 2		26	1	2	2	1	2	1	1	525	2	1	1	1	1
Diana		26	1	3	2	1	1	2	2	635	1	1	1	1	1
Yasmin		30	2	3	2	1	1	1	2	1495	1	1	1	1	1
Dhanalakshmi		32	1	3	2	1	1	2	2	1410	2	1	1	1	1
Usharani		30	1	3	2	1	1	2	2	1285	2	1	1	1	1
Chandrakala		29	1	3	1	1	2	2	1	815	1	1	1	1	3

Priya 1		27	1	2	2	1	1	2	2	700	2	1	2	1	1
Sujatha		31	2	4	2	2	1	2	2	1440	1	2	1	1	3
Chandrakala		26	2	4	2	1	1	1	3	1325	1	1	1	1	1
Monika		30	1	3	2	1	1	2	2	1310	3	1	1	1	3
Valarmathi		30	1	2	1	1	1	1	2	1115	2	1	1	1	1
Ananthi		33	4	3	2	2	1	1	3	2770	1	2	1	1	1
Kowsalya		27	1	3	2	1	1	1	2	700	1	1	1	1	1
Muruganandhi 2		29	2	3	2	2	1	2	2	1380	1	2	2	1	1
Ramya		30	1	4	2	1	1	2	2	1250	1	3	1	1	3
Jayalakshmi		31	4	3	2	1	1	1	2	1940	2	2	1	1	1
Devi		26	1	2	1	1	1	1	2	945	1	1	1	1	1
Shakila		31	3	3	2	2	1	1	2	1650	1	2	1	1	1
Shakila		33	1	3	2	1	2	1	1	1250	1	1	1	1	1
Poongavanam 2		33	1	3	1	2	2	2	1	1245	1	1	1	1	1
Farhana		29	4	3	2	1	1	1	2	1245	1	3	1	1	3
Sujatha		31	2	4	2	2	1	2	2	1440	1	2	1	1	3
Chandrakala		26	2	4	2	1	1	1	3	1325	1	1	1	1	1
Amudha	2	32	1	3	1	1	2	1	1	1480	1	1	1	1	1
Ramya	2	32	1	4	2	2	1	1	2	1664	1	2	1	1	1
Nalini	2	29	1	2	1	1	1	1	3	1750	1	1	1	1	1
Kokila	5	33	4	3	2	1	1	1	2	1740	1	1	1	1	1
Nirmala	5	34	1	3	1	2	2	1	1	1530	1	2	1	1	1
Anitha	5	29	1	3	1	1	1	1	2	1100	1	3	1	4	2
Vasuki	5	34	1	4	1	1	2	2	1	1620	1	1	1	1	1
Suganthi 1	1	32	1	3	1	1	1	1	2	1700	1	3	3	4	3
Suganthi 2	1	32	1	3	1	1	1	1	2	1600	1	3	3	4	3
Mahalakshmi 1	2	29	1	4	2	1	1	2	2	1300	1	1	2	1	1
Priyanka	3	32	1	3	2	1	2	2	1	1100	1	3	1	2	2
Christiya	5	32	3	1	1	1	2	1	2	1440	1	1	1	1	1
Girija	4	31	1	3	2	1	1	1	2	1685	1	1	1	1	1
Roja	4	30	1	3	1	1	1	1	2	1320	1	3	1	2	1
Sumathi	4	31	4	3	1	2	1	2	2	1120	1	2	1	1	1
Kanimozhi	4	34	2	3	2	1	1	1	2	2400	1	4	1	1	1
Ammu	4	31	1	3	1	1	1	2	2	1450	1	1	1	1	1
Shailaja	2	31	1	1	2	1	1	2	2	1270	1	1	1	1	1
Chinnakka	5	32	4	3	1	1	1	1	2	1700	1	1	1	1	1
Kanimozhi	3	32	1	3	1	1	1	1	2	1550	1	1	1	1	1
Priya	2	34	1	3	2	1	2	2	1	1390	1	1	1	1	1
Saraswathi	5	31	1	3	1	2	1	1	2	1340	2	2	1	1	1
Bharathi	1	29	1	4	2	1	1	1	2	1200	1	1	1	1	1
Padmavathy	4	32	1	3	1	1	1	1	2	1630	1	1	1	1	1
Govindammal	6	33	3	3	1	1	2	2	1	1490	1	1	1	1	1
Dhanalakshmi	5	32	1	4	1	1	1	2	2	1900	1	1	1	1	1
Samayapurathal	4	30	1	3	1	1	1	1	2	1400	1	1	1	1	1

Anitha 1	5	32	1	4	1	1	1	1	2	1600	1	1	2	1	1
Anitha 2	5	32	1	4	1	1	2	2	2	1460	1	1	2	1	1
Arunakumari	2	32	4	3	2	2	1	2	2	1600	1	2	1	1	1
Sweetarani	4	31	1	2	2	1	1	1	2	1310	1	1	1	1	1
Bakkiyam	5	31	1	3	1	1	1	2	2	1435	1	1	1	1	1
Mohana	1	32	1	4	2	1	1	1	2	1965	2	1	1	1	1
Gomathi	5	31	4	2	1	3	1	2	2	1420	1	2	1	1	1
Lalitha 1	4	32	1	3	2	2	2	1	2	1380	1	2	3	1	1
Lalitha 2	4	32	1	3	2	2	2	1	1	1350	1	2	3	1	1
Lakshmi 1	5	29	1	3	2	1	1	1	2	1080	1	1	2	1	1
Priya	4	29	1	3	1	1	1	1	2	1455	2	3	1	2	1
Saritha 1	5	31	4	4	2	2	1	1	2	1405	3	2	2	1	1
Saritha 2	5	31	4	4	2	2	1	1	2	1700	2	2	2	1	1
Bhavani 1	5	31	1	3	2	1	1	1	2	1470	1	1	1	1	1
Bhavani 2	5	31	1	3	2	1	1	1	2	1120	1	1	1	1	1
Shakila	5	29	2	3	2	2	1	1	2	1130	1	2	1	1	1
Ammu	3	29	1	4	2	1	1	2	2	1100	1	1	1	1	1
Bhuvana	3	34	3	3	2	1	1	1	3	3305	1	3	1	1	1
Revathi	5	34	1	4	2	1	2	2	1	1595	2	1	1	4	1
Jayanthi	5	34	3	3	1	1	1	2	2	2000	1	1	1	1	1
Manju 2	5	34	4	3	2	1	1	2	2	2100	1	1	2	1	1
Manju 1	5	34	4	3	2	1	1	2	1	1640	1	1	2	2	1
Janet Julie	2	34	1	2	2	1	2	1	1	1640	2	3	1	2	2
Chitra	4	33	1	3	1	2	1	1	2	1805	1	2	1	1	1
Sowthamani	1	32	4	4	2	1	1	1	2	1810	1	4	1	1	1
Viji	2	32	1	3	2	1	2	1	1	1000	2	3	1	1	3
Revathi 1	2	29	1	3	2	2	1	1	2	1265	1	2	2	1	1
Jagadeeswari 1	1	31	4	3	2	1	1	2	2	1395	1	1	2	1	1
Jagadeeswari 2	1	31	4	3	2	1	1	2	2	1320	1	1	2	1	1
Rathi	5	34	4	4	2	2	1	1	2	2275	1	2	1	1	1
Kalaiarasi	2	33	3	3	1	2	1	2	2	2215	1	2	1	1	1
Vijayalakshmi 2	5	34	1	3	2	1	2	1	1	1360	1	3	4	1	2
Vijayalakshmi 1	5	34	1	3	2	1	2	1	1	1245	1	3	4	1	2
Priya	6	31	1	2	1	5	1	1	2	1470	1	2	1	1	2
Supriya	5	34	1	3	1	1	1	1	2	1960	1	1	1	1	1
Shanthi	2	33	1	3	2	2	1	1	2	2060	1	2	1	1	1
Malini	4	34	1	3	2	1	1	1	2	2180	1	1	1	1	1
Dhanalakshmi 1	2	34	1	3	1	1	2	1	1	1365	1	3	2	1	1
Dhanalakshmi 2	2	34	1	3	1	1	1	2	2	2160	1	3	2	1	1
Usha	2	33	1	3	1	2	1	1	2	1870	1	2	1	1	1
Malathi 1	4	33	1	3	2	2	1	2	2	1770	1	2	2	1	1
Malathi 2	4	33	1	3	2	2	1	2	2	1925	1	2	2	1	1
Kavitha rani	1	30	1	3	2	2	1	1	2	1665	1	2	1	1	1
Surya	4	33	1	3	2	2	1	1	2	2155	1	2	1	1	1

Anbarasi	2	33	4	3	2	2	1	1	2	2000	1	2	1	1	1
Kavitha	4	33	1	3	1	1	1	2	2	1840	1	3	1	2	3
Rekha	5	34	3	3	1	2	2	1	1	1700	1	2	1	1	1
Nagalakshmi	4	33	2	3	1	2	1	2	2	1785	1	2	1	1	1
Amudha	6	31	4	3	1	2	1	1	2	1370	1	2	1	1	1
Vijayalakshmi 1	1	32	2	3	2	2	1	1	2	1670	1	2	2	1	1
Vijayalakshmi 2	1	32	2	3	2	2	1	2	1	1220	1	2	2	1	1
Tamilarasi	7	34	2	3	1	1	2	2	1	1345	1	3	1	1	3
Pushpa 1	3	31	1	3	2	1	1	2	2	1415	1	1	2	1	1
Pushpa 2	3	31	1	3	2	1	1	2	2	1705	1	1	2	1	1
Abirami	5	32	1	3	2	1	2	1	1	930	1	3	1	1	1
Sripriya	3	28	4	4	2	2	1	1	2	1245	1	2	1	1	1
Revathi	5	33	1	3	1	1	2	2	2	1675	1	3	1	1	1
Sangeetha 1	5	34	4	3	1	2	2	1	1	1280	1	2	2	1	1
Devi	5	33	4	3	1	1	1	2	2	1760	3	3	1	4	2
Priyanka	3	34	1	3	2	2	1	1	2	2130	1	2	1	1	1
Banupriya	4	31	1	4	2	2	2	1	1	1205	1	2	1	2	1
Neethidevi 1	3	32	1	3	2	1	2	2	1	1305	1	3	3	2	3
Anitha	5	29	4	1	1	1	1	1	2	1590	1	3	1	1	3
Indhumathi	3	33	3	3	2	1	2	1	1	1470	1	3	1	1	3
Srividhya	5	33	4	3	2	1	2	2	1	1370	1	3	1	1	3
Siddhi Fathima	1	32	4	4	2	2	1	1	2	1625	1	2	1	1	1
Valarmathi	5	33	3	3	2	5	1	1	2	2135	1	2	1	1	1
Eswari	5	32	1	4	2	1	1	2	2	2010	1	1	1	2	1
Indra	4	33	1	3	2	2	1	1	2	1965	1	2	1	2	1
Latha	7	34	3	2	1	1	1	1	2	2070	1	1	1	1	1
Latha 1	6	31	1	4	2	2	1	2	2	1485	1	2	2	1	1
Latha 2	6	31	1	4	2	2	1	2	2	1235	2	2	2	1	1
Sasikala 1	4	33	4	4	2	2	1	1	2	1635	1	2	2	1	1
Sasikala 2	4	33	4	4	2	2	1	1	2	1690	1	2	2	1	1
Shakila	4	31	4	3	1	2	1	1	2	1650	1	2	1	1	1
Vinodhini	2	30	1	4	2	2	1	2	2	1445	1	2	1	1	1
Manjula	2	32	4	3	2	2	1	2	2	1870	1	2	1	1	1
Meena 1	2	28	2	3	2	1	1	1	2	1510	1	1	2	1	1
Meena2	2	28	2	3	2	1	1	2	2	1235	1	1	2	1	1
Latha	4	34	1	3	1	2	2	2	2	1700	1	2	1	1	1
Deepa	5	33	1	3	1	1	1	2	2	1965	1	3	1	2	3
Chinna nagamma	5	34	3	3	1	1	1	1	2	2095	1	1	1	1	1
Muruganandhi 1	6	30	3	4	2	2	1	2	2	1415	1	2	2	1	1
Jothi	5	30	4	4	2	1	1	2	2	1150	2	1	1	1	1
Anitha	5	32	2	3	2	3	1	1	2	1550	1	3	1	1	3
Jeyalakshmi	5	28	3	3	2	1	1	2	2	1060	3	1	1	1	1
Gomathi	4	34	4	3	1	2	2	1	1	1500	3	2	1	2	1
Ilamathi 2	5	33	2	4	2	1	1	2	2	2040	2	3	4	1	3

Ilamathi 1/3	5	33	2	4	2	1	1	2	2	1715	1	3	4	1	3
Saritha	4	30	1	3	1	2	1	2	2	1430	1	2	1	1	1
Grace	3	29	4	3	2	3	1	1	2	1505	1	1	1	2	1
Rani	2	28	2	3	2	1	1	2	2	1100	1	3	1	1	3
Deepa 1	4	34	2	2	1	1	1	1	2	1970	1	1	3	1	1
Saraswathi	5	34	3	3	1	1	2	1	1	1580	1	1	1	1	1
Vanaja	4	33	4	3	2	2	1	1	2	1900	1	2	1	1	1
Kanagavalli	5	30	3	3	2	1	2	2	2	1045	2	3	1	1	3
Kavitha 3	5	34	1	4	2	2	2	1	1	1895	1	2	4	1	1
Kavitha 2	5	34	1	4	2	2	2	1	1	1400	1	2	4	1	1
Selvi	5	30	1	3	2	1	1	1	2	1570	1	1	1	1	1
Rakhi	3	34	1	3	2	2	1	1	2	1960	1	2	1	1	1
Valliammal 1	2	33	1	1	2	1	1	2	2	1500	1	1	2	1	1
Valliammal 2	2	33	1	1	2	1	2	2	1	1090	1	1	2	1	1
Malini	5	34	1	4	2	1	2	1	1	1645	1	3	1	1	1
Ishwarya	5	34	1	3	2	1	2	1	1	1630	1	3	1	1	3
Divya	2	32	1	2	2	1	2	2	1	1000	1	3	1	1	2
Uma Maheswari 1	5	33	4	2	1	2	1	2	2	1775	1	2	2	1	1
Banupriya	6	34	4	1	1	1	2	1	1	1455	1	1	1	1	1
Vennila	2	31	3	2	1	1	1	2	2	1935	1	1	1	1	1
Jaya	5	31	3	3	1	2	2	2	1	1135	1	2	1	1	1
Durga	5	32	1	3	1	1	1	2	2	1805	1	1	1	1	1
Kavitha	2	33	1	3	2	2	2	2	1	1605	1	2	1	1	1
Indra 1	5	31	1	3	2	2	1	1	2	1220	2	2	2	1	1
Indra 2	5	31	1	3	2	2	1	1	1	1060	1	2	2	1	1
Anu	4	32	1	3	2	1	1	1	2	1780	1	1	1	1	1
Jeya	5	32	3	3	2	1	1	2	2	1860	1	1	1	1	1
Valarmathy	2	33	1	4	2	1	1	2	2	1815	1	1	1	1	1
Parveen 1	5	31	1	3	2	2	1	2	2	1545	1	2	2	1	1
Banupriya	6	34	1	2	1	2	2	1	1	1455	1	2	1	1	1
Parameswari	4	33	3	3	2	1	1	1	2	2470	1	1	1	1	1
Malini	4	32	3	3	1	1	1	1	2	1780	1	1	1	1	1
Sai Vishnu Priya	2	30	4	4	1	1	1	1	2	1290	1	1	1	4	1
Prasanna	5	34	2	3	2	1	2	2	1	1455	1	3	1	1	3
Kalaivani	5	34	2	3	2	1	1	2	3	2850	1	1	1	1	1
Mahalakshmi	5	31	1	2	1	2	1	2	2	1260	1	2	1	1	1
Anitha 1	2	31	2	3	2	1	1	2	2	1530	1	1	3	1	1
Anitha 2	2	31	2	3	2	1	1	2	2	1715	1	1	3	1	1
Sasikala	5	33	4	3	2	1	2	1	2	1885	1	1	1	1	1
Durga	5	32	1	3	2	1	2	2	1	1195	1	3	1	1	2
Vaitheeswari	4	29	1	3	2	1	2	1	2	1380	1	1	1	4	1
Palpandi 1	5	30	1	3	1	1	1	1	2	1500	1	1	3	1	1
Palpandi 2	5	30	1	3	1	1	1	1	2	1385	1	1	3	1	1
Bharathi 1	2	28	1	3	2	2	1	2	2	930	1	2	4	1	1

Bharathi 2	2	28	1	3	2	2	1	2	2	980	1	2	4	1	1
Bharathi 3	2	28	1	3	2	2	1	2	2	895	1	2	4	1	1
Anitha 1	2	31	1	3	2	2	1	1	2	1490	1	2	2	1	1
Pattu 1	4	29	4	3	2	1	1	2	2	1145	1	1	2	4	1
Pattu 2	4	29	4	3	2	1	1	1	2	1135	2	1	2	4	1
Nirosha	4	33	1	3	2	2	1	2	2	1870	1	2	1	1	1
Jansi rani	3	33	3	3	2	2	1	2	2	2000	1	2	1	1	1
Sumathy	6	30	1	2	1	4	1	1	3	2210	1	1	1	1	1
Selvakumari	3	32	4	4	2	2	1	1	2	1530	1	2	1	1	1
Elamozhi	5	32	2	3	1	1	1	2	2	1475	1	1	1	1	1
Nirmala	3	33	1	3	2	3	1	1	2	2105	1	1	1	1	1
Vasanthakumari	5	34	1	3	1	2	1	1	2	1925	1	2	1	1	1
Vijayashanthi	3	34	4	3	2	1	1	1	3	3195	1	1	1	1	1
Anitha 2	2	32	1	4	2	1	2	1	1	1140	1	1	3	1	1
Malliga	5	28	3	2	1	1	1	1	2	1000	1	1	1	1	1
Revathy 1	5	31	1	3	2	1	2	2	1	1250	1	3	3	1	1
Malini	4	34	1	3	2	1	2	1	1	1655	1	3	1	2	1
Nandhini 1	2	33	1	3	2	2	1	2	2	1795	1	2	2	1	1
Haripriya 1	5	34	1	3	1	1	2	2	1	1650	1	3	1	1	2
Gowri	6	33	1	3	1	2	1	2	2	2010	1	2	1	1	1
Lakshmi priya 1	2	34	1	3	1	1	2	1	2	1915	1	1	2	1	1
Lakshmi priya 2	2	34	1	3	1	1	2	2	1	1685	1	1	2	1	1
Sridevi	2	32	4	3	1	1	2	1	1	1300	1	3	1	2	1
Chitramani	2	29	1	4	2	1	1	2	2	1170	1	1	1	1	1
Elakkiya	5	30	4	3	2	1	1	1	2	1670	1	1	1	4	1
Chitra	2	31	2	3	2	1	1	1	2	1640	1	1	1	1	2
Pushpalatha	2	33	1	4	2	1	2	1	1	1135	1	3	1	1	1
Dhatchayani	5	32	1	3	1	2	1	2	2	1630	1	2	1	1	1
Parveen 2	5	31	1	3	2	1	1	2	2	1265	1	2	2	2	1
Kanmani	5	31	1	3	2	2	1	1	2	1875	1	2	1	1	1
Dharani	5	33	1	3	2	2	1	1	2	1850	1	2	1	1	1
Bhavani	2	31	1	3	2	1	2	1	1	935	1	3	1	1	2
Vijayalakshmi 1	4	32	1	3	1	1	2	1	1	1360	1	1	3	1	1
Ashwini	2	34	3	3	2	1	2	2	1	1375	1	3	1	1	3
Priya	5	33	1	4	2	1	2	2	1	1110	2	3	1	2	3
Sharadha	5	33	2	3	1	2	1	2	2	2010	1	2	1	1	1
Divya	2	29	3	2	2	1	2	2	2	810	1	3	1	1	1
Bharathi	5	30	3	3	1	1	1	2	2	1340	1	1	1	1	1
Jothi	5	30	1	3	1	2	1	2	2	1140	1	2	1	3	1
Logapriya	5	32	3	3	1	2	1	2	2	1535	1	2	1	1	1
Kamala	1	33	2	3	2	2	1	1	2	2395	1	2	1	1	1
Mohanaselvi	4	28	1	3	2	2	1	1	2	1030	1	2	1	1	1
Priya	5	28	1	2	2	3	1	2	2	1190	1	1	1	1	1
Mahalakshmi 1	2	32	1	3	2	2	1	2	2	1770	1	2	2	1	1

Mahalakshmi 2	2	32	1	3	2	2	1	1	2	1895	1	2	2	1	1